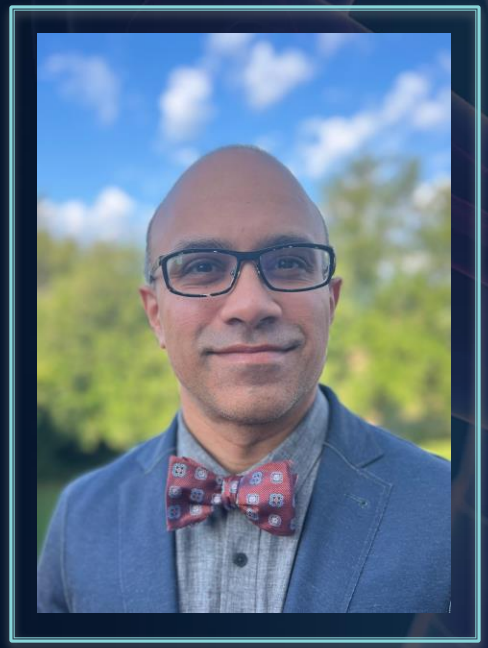
Optimizing Ulcerative Colitis Management

Navigating Challenges and Enhancing Outcomes in Managed Care

SUPPORTED BY AN EDUCATIONAL GRANT FROM LILLY.

CME OUTFITTERS



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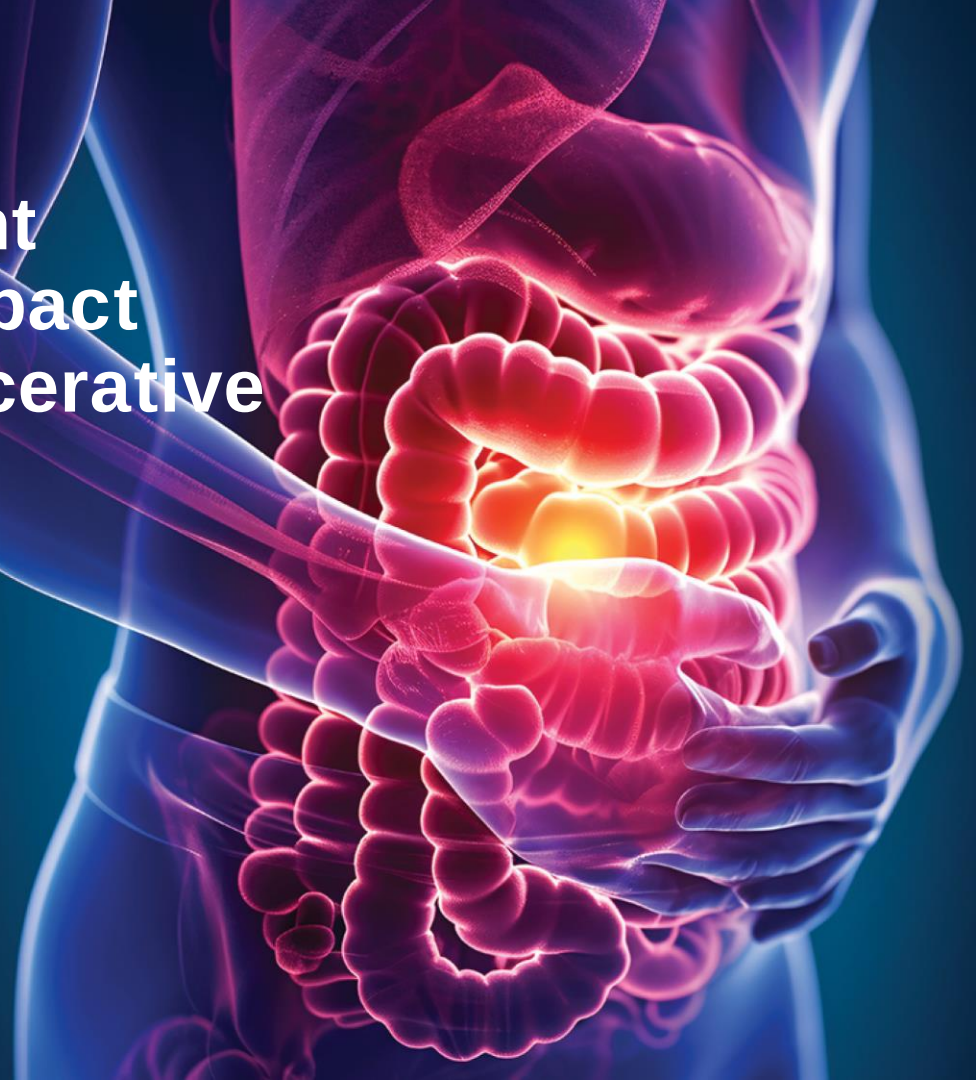
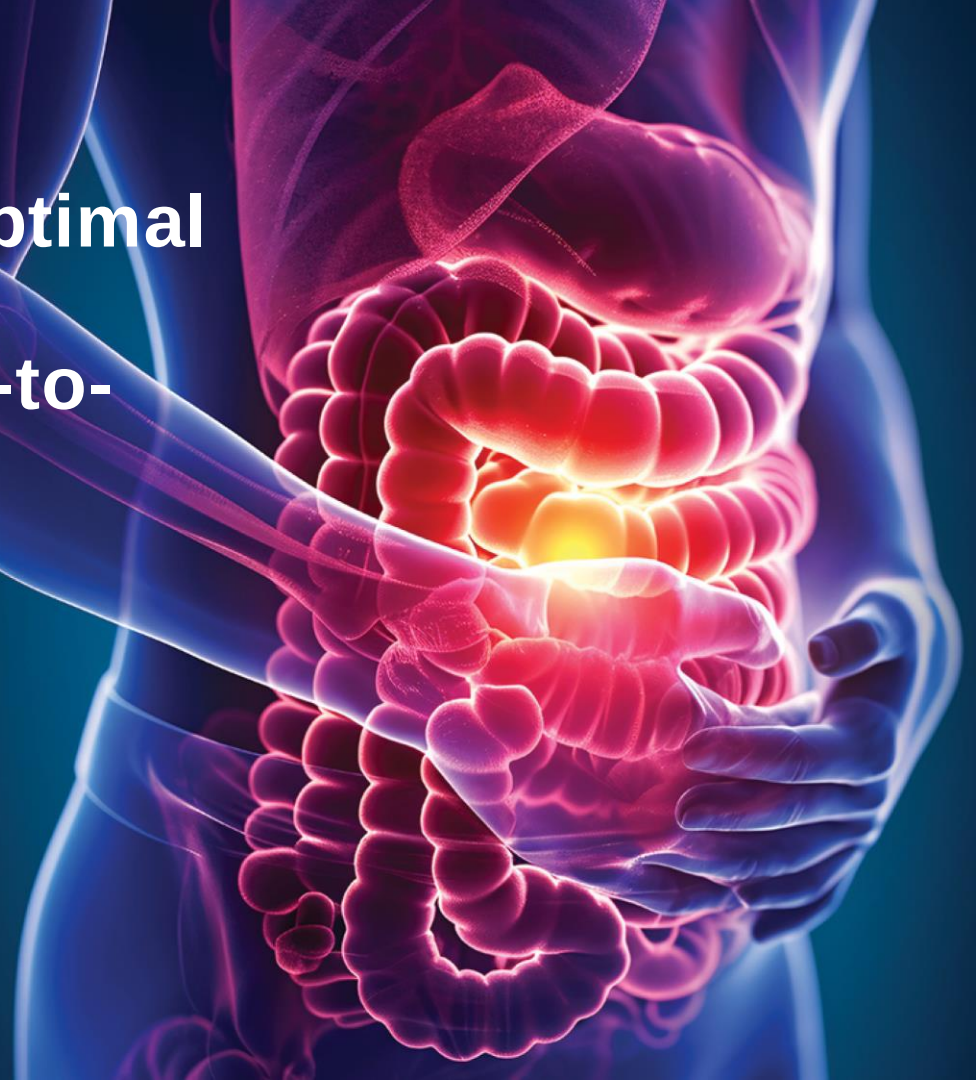
Identify how delays in diagnosis and treatment initiation negatively impact patient outcomes in Ulcerative Colitis (UC)

LEARNING OBJECTIVE 1



Evaluate the economic consequences of suboptimal advanced treatment in patients with moderate-to-severe UC

LEARNING OBJECTIVE 2

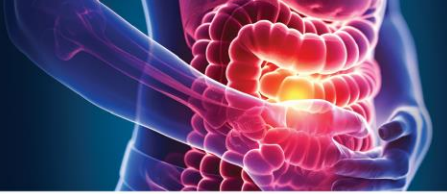


Incorporate the latest data and guidelines for the treatment of UC into population health decisions

LEARNING OBJECTIVE 3

Overcoming Treatment Delays for Ulcerative Colitis

Audience Response



Which of the following barriers to insurance coverage for advanced therapy do patients with UC face most often?

A. Requirement for step therapy
B. Medication denial
C. Prior authorization
D. Mandated medication switch
E. I don’t know

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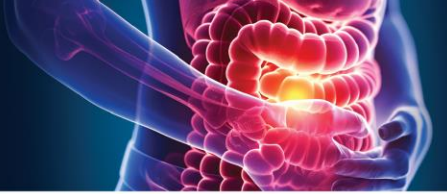
Audience Response



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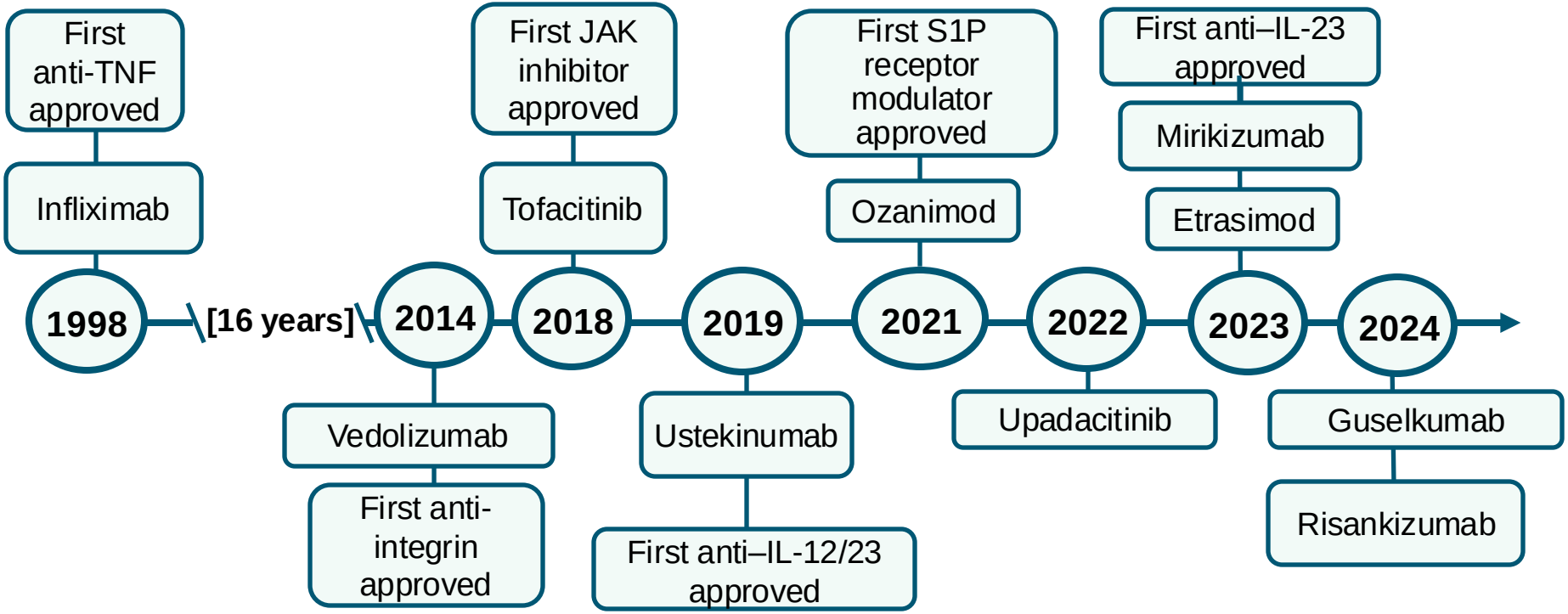
Evolution of UC Treatment Landscape

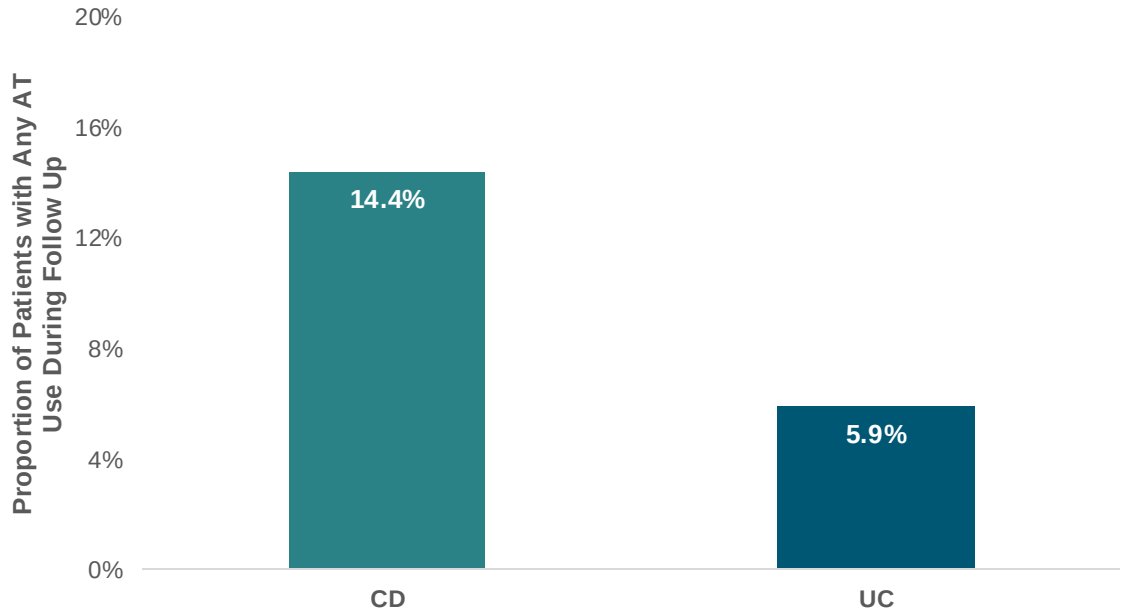


CD = Crohn's disease; IBD = inflammatory bowel disease; IL = interleukin; JAK = Janus kinase; S1P = sphingosine-1-phosphate; TNF = tumor necrosis factor; UC = ulcerative colitis.

Modified from Pouillon L, et al. *Nat Rev Gastroenterol Hepatol.* 2021;18(2):143.

CME OUTFITTERS

Lag in Use of Advanced Treatments in IBD

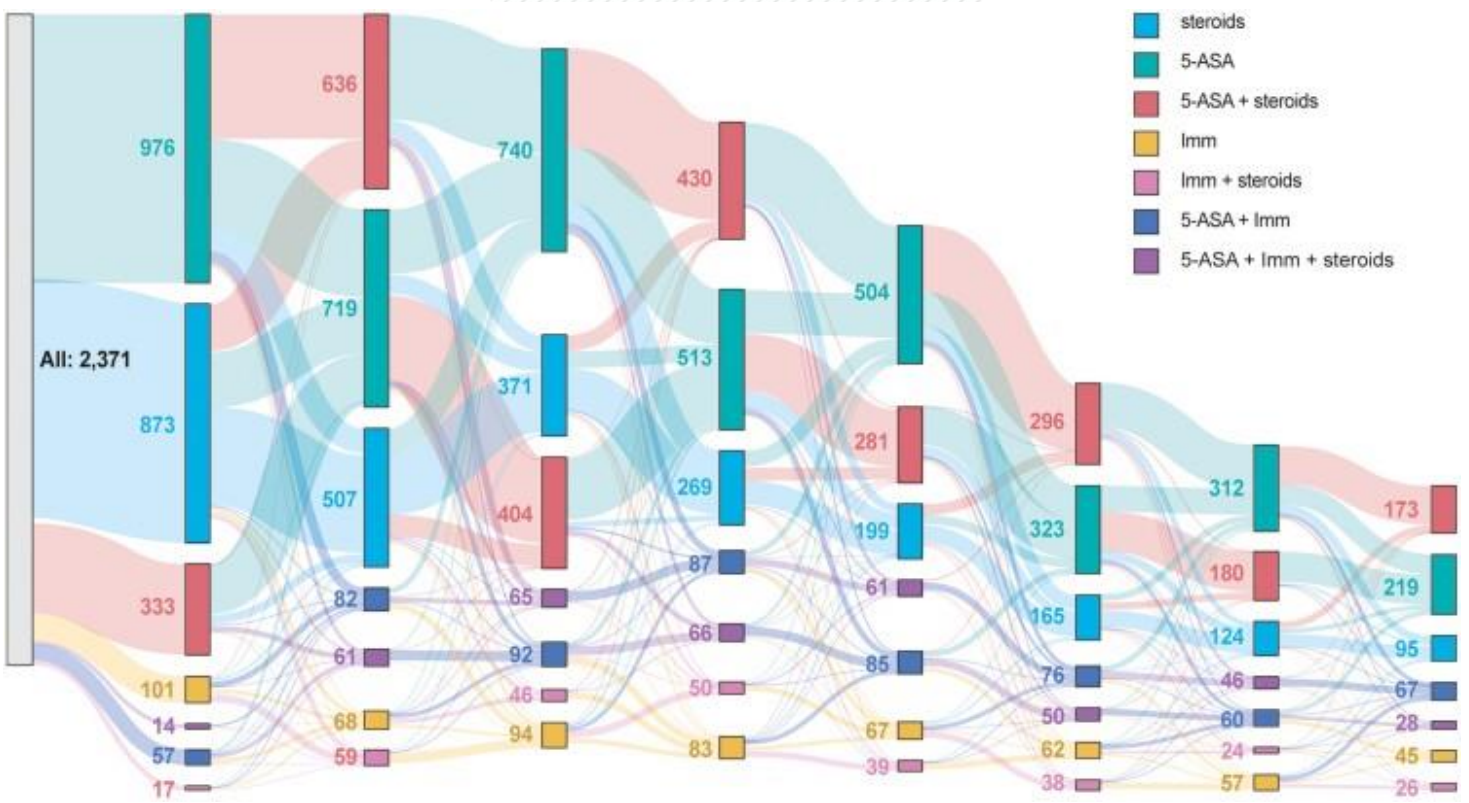


AT = advanced treatment

Siegel CA, et al. *Crohns Colitis 360*. 2024 Aug 20;6(3).

CME OUTFITTERS

Patients with UC Are Treated with 5+ Rounds of Conventional Therapy Before They Receive an Advanced Therapy



Siegel CA, et al. *Crohns Colitis 360*. 2024;6(3).

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Discordance Between Treatment Guidelines and Insurance Guidelines

- Historically treatment of UC was done in a gradual, step-up manner
- This approach is no longer supported by treatment guidelines, which favor early initiation of biologic therapy
  - "In adult outpatients with moderate-severe ulcerative colitis, the AGA suggests early use of biologic agents with or without immunomodulator therapy, rather than gradual step up after failure of 5-aminosalicylates."[1]
- **98%** insurance pathways still require failure on multiple lines of therapy before initiating biologics[2]

AGA = American Gastroenterological Association

1. Feuerstein JD, et al. *Gastroenterol.* 2020;158(5):1450-1461. 2. Yadav A, et al. *Inflamm Bowel Dis.* 2017;23:853-857.

Patient Experience With Treatment Delays: IBD Partners Insurance Survey

72% of patients experienced an insurance-mandated barrier to treatment

- Prior Authorization (51%)
- Medication Denial (15%)
- Step Therapy (11%)
- Medication Change (8%)

Impact of barriers on outcomes

Prior Authorization

- Increased corticosteroid rescue

Medication switches

- Continued disease activity

Medication denials

- More UC-related surgery

Constant BD, et al. *Am J Gastroenterol.* 2024 May;119(5):655-660.

Impact of Prior Authorization

Physician-Reported Impact on Clinical Practice

- **97%** worsens care
- **87%** limits ability to provide optimal care
- **61%** delayed prescriptions

Healthcare Utilization

- **84%** of physicians have hospitalized patients to expedite prescriptions

Patient Outcomes

- **82%** disease activity-related hospitalization
- **2%** surgery
- **1%** death

Constant BD, et al. *Clin Gastroenterol Hepatol.* 2024;22(2):423-426.

Impact of Treatment Delays: TARGET-IBD

Early vs Delayed Initiation of Advanced Therapy in Patients with Moderate Ulcerative Colitis

Time to remission:

- 10.8 months for early initiators
- 15.4 months for delayed initiators

Early initiation of advanced therapy associated with increased likelihood of endoscopic remission (HR = 2.44)

Patients initiating advanced therapy within the first year after diagnosis were **3x more likely to achieve endoscopic remission** than those initiating more than 2 years after diagnosis

HR = hazard ratio; IBD = inflammatory bowel disease

Rubin DT, et al. *Am J Gastroenterol.* 2023;118(12S):S3-S4.

Strategies to Minimize Insurance Barriers

Barriers	Solutions
Prior authorization, step therapy, and restricted access to treatment	Create national appeal process standards
Prohibitive drug costs	Reform federal payment rules to reduce out-of-pocket costs using copay assistance programs
Forced nonmedical switching	Adopt a national process and ethical standards for benefits policy development. Eliminate artificial restrictions based on step therapy and FDA labels
Coverage gaps in disease monitoring	Cover drug and disease activity monitoring
Inadequate coverage for multidisciplinary care	Embrace holistic multidisciplinary care. Encourage new models of care delivery. Promote patient activation and shared decision-making.
Limited access to IBD specialists	Incorporate risk stratification, tailored treatment paradigms
Inequality and intersecting identities with IBD	Engage the cause and effects of inequality in care

FDA = Food and Drug Administration; IBD = inflammatory bowel disease

Sofia MA, et al. *Clin Gastroenterol Hepatol.* 2024;22(5):944-955.

Prior Authorization Reform: AMA Position

- Volume reduction (elimination of prior authorization requirements for regularly approved care, gold-carding programs)
- Quick response times (24 hours for urgent, 48 hours for nonurgent)
- Prohibit retroactive denials for preauthorized care
- **Make prior authorizations valid for >1 year, regardless of dose changes**
  - **Valid for full length of treatment for chronic conditions**
- Public release of insurer's prior authorization data
- Prohibition of requiring prior authorizations when patients switch plans before they can get coverage for ongoing care

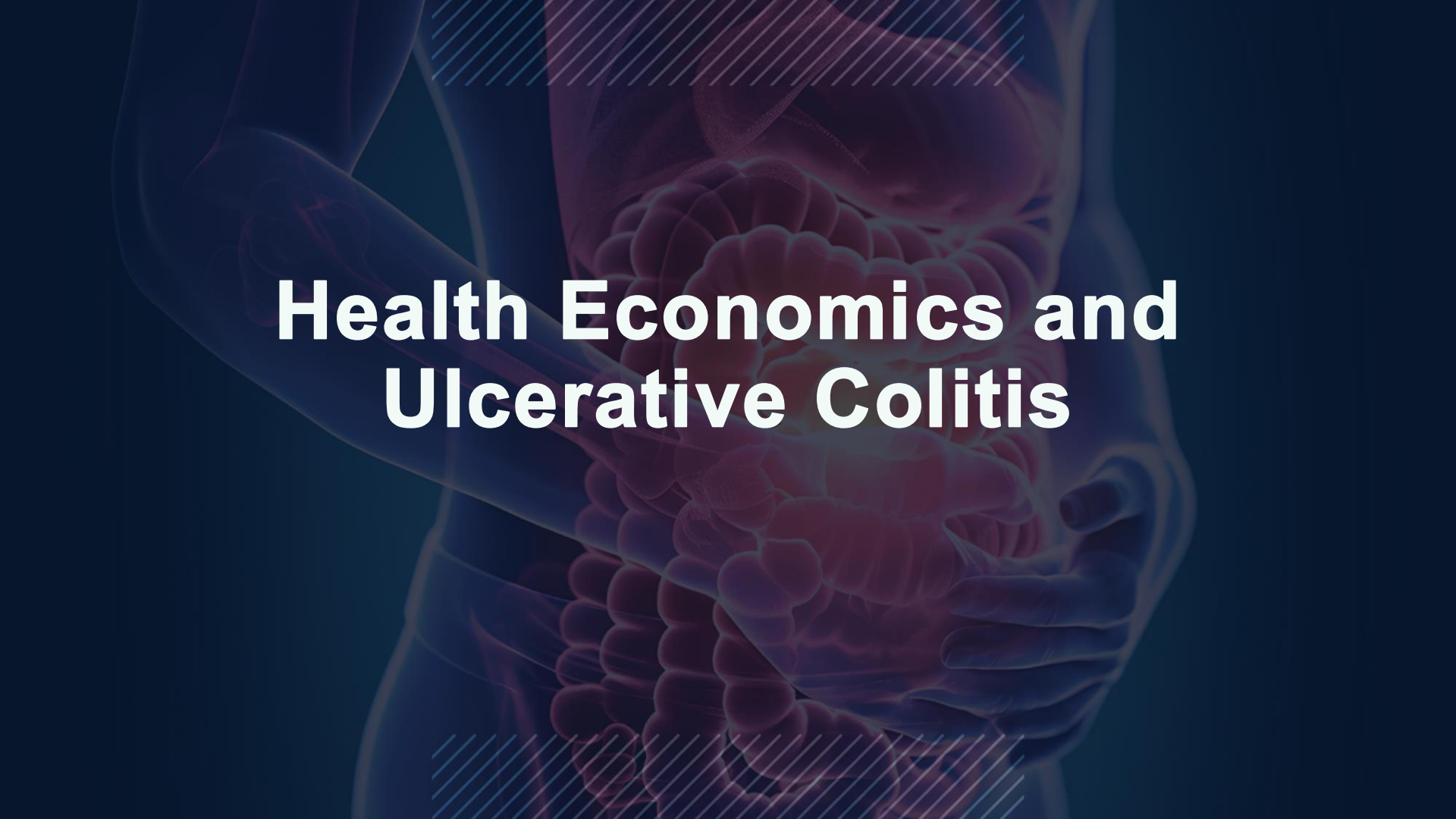
American Medical Association [AMA]. *Advocacy in action: Fixing prior authorization.* 2024. https://www.ama-assn.org/practice-management/prior-authorization/advocacy-action-fixing-prior-authorization

Impact of novel therapies on patient outcomes—importance of advanced therapy

Faculty Discussion

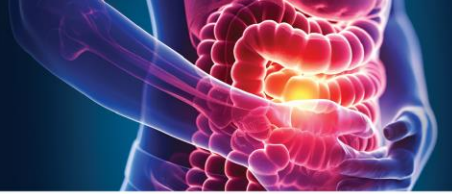
Role of managed care, payors, and clinicians within integrated delivery systems in ensuring patients have access to the optimal treatment

Faculty Discussion

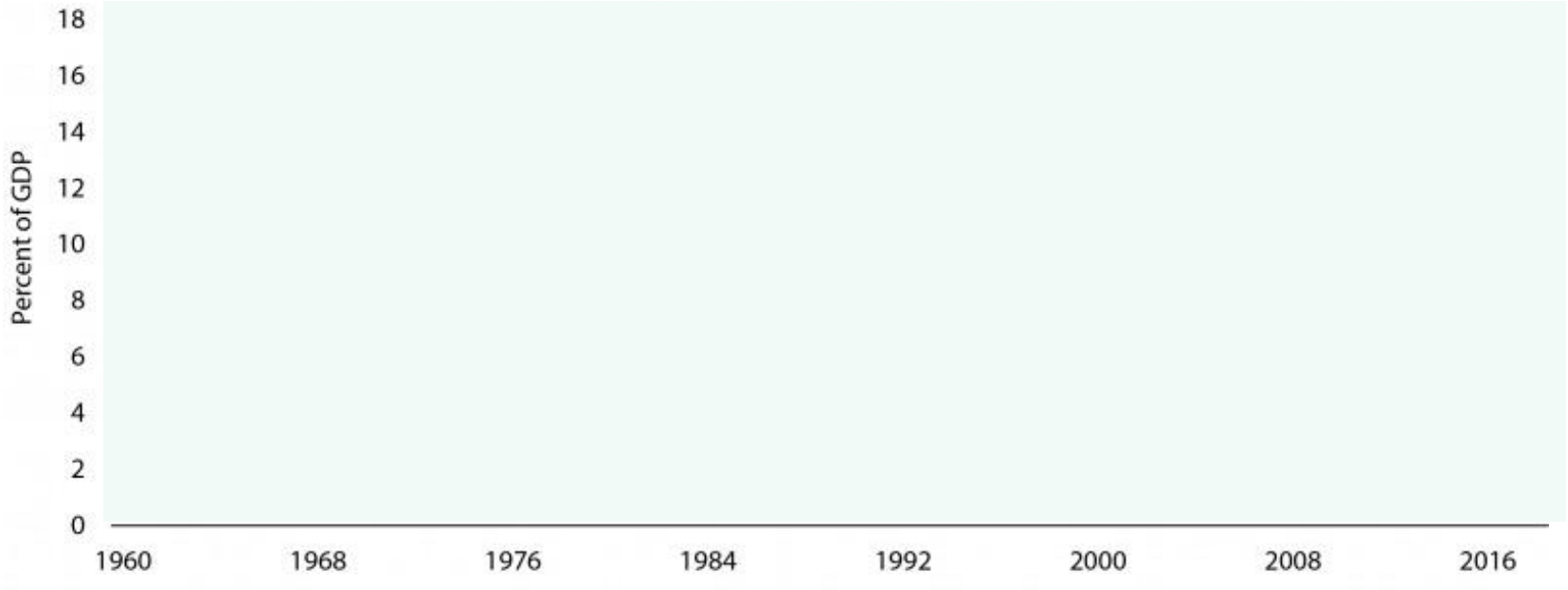


Health Economics and Ulcerative Colitis

Increase in Healthcare Spending



US Healthcare Expenditures as a Share of GDP, 1960-2018



CMS 11960-2018.

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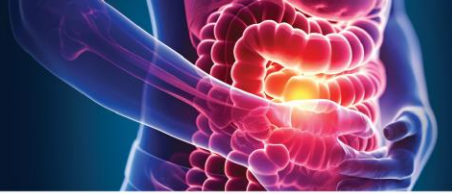

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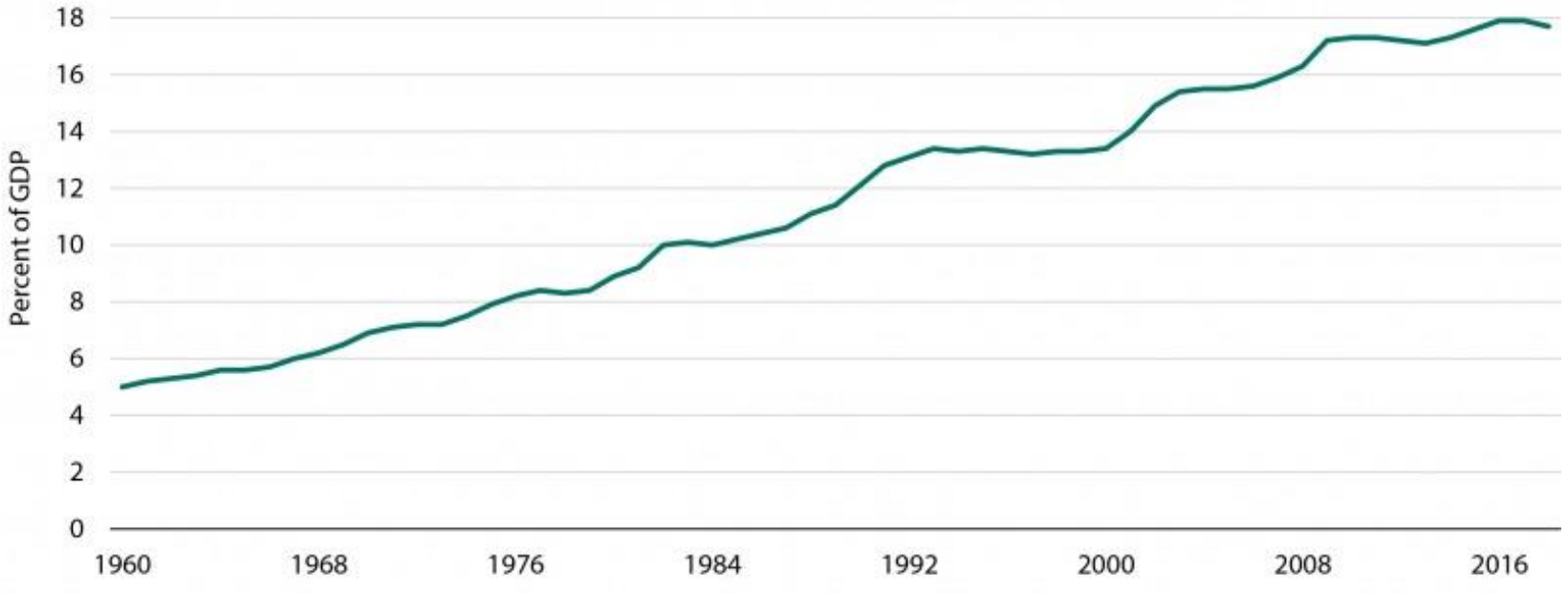

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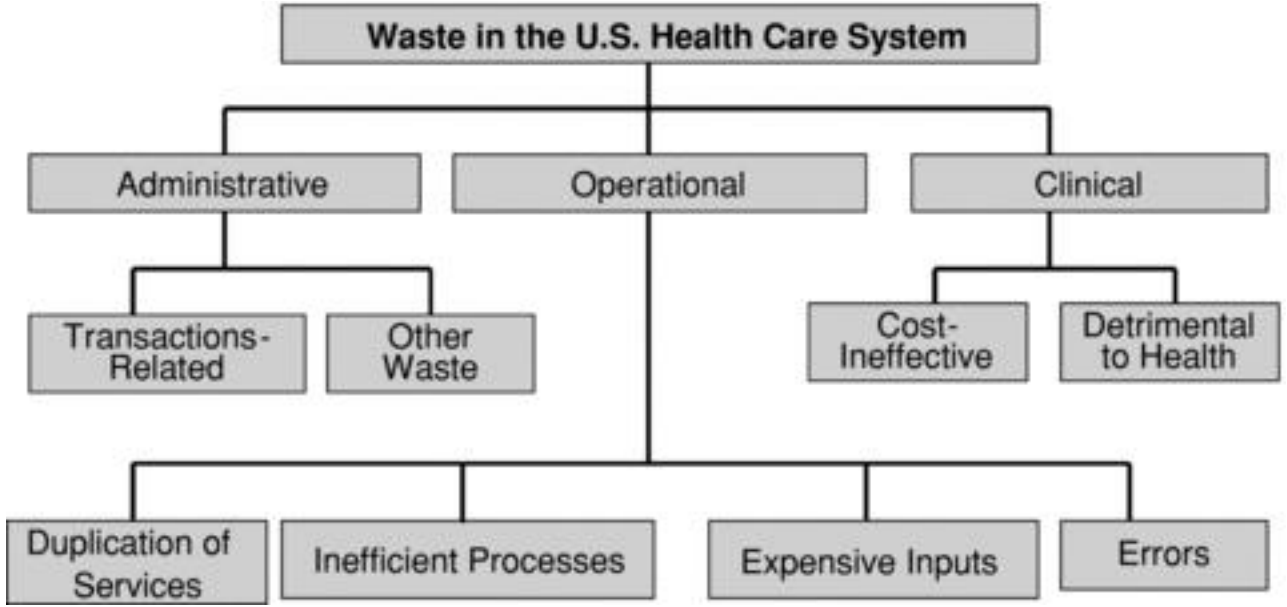
Waste in the US Healthcare System: A Conceptual Framework



Bentley TGK, et al. *Millbank Q.* 2008 Dec;86(4):629-59.

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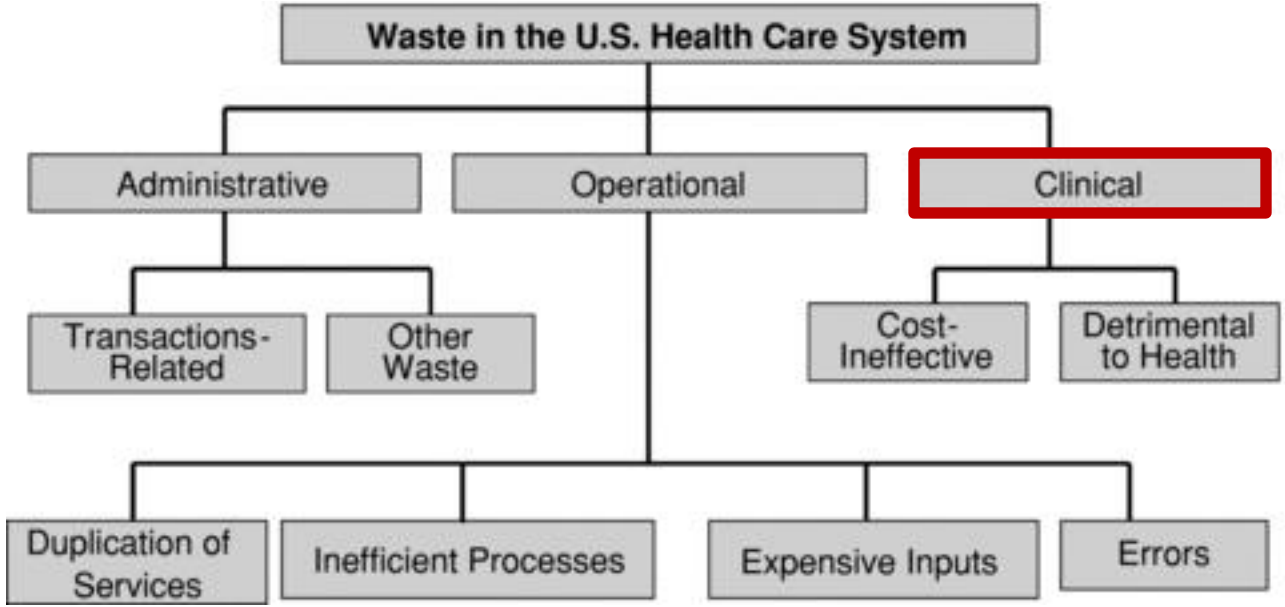

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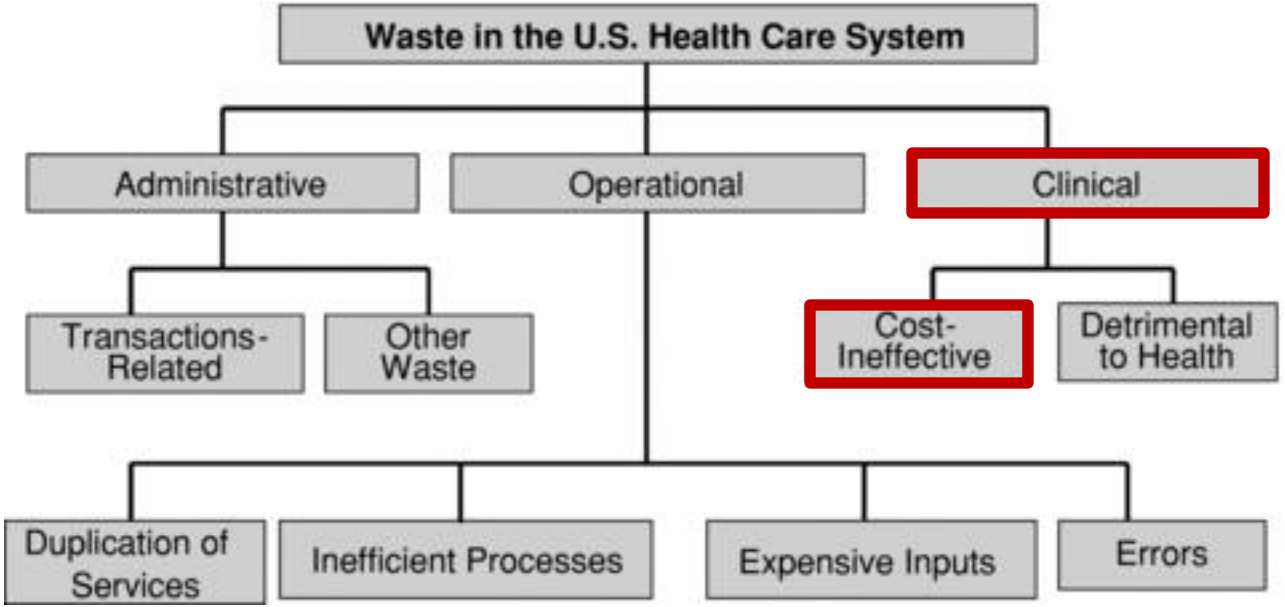

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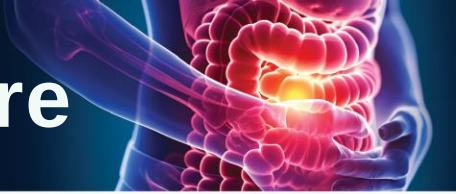

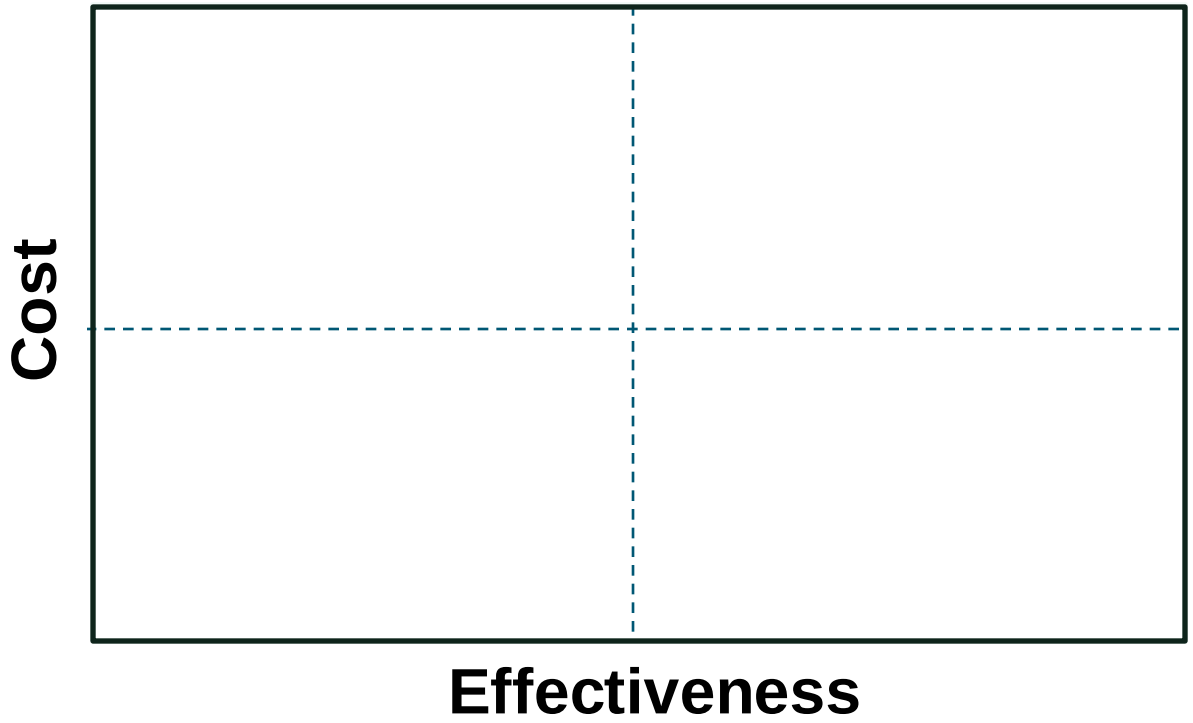

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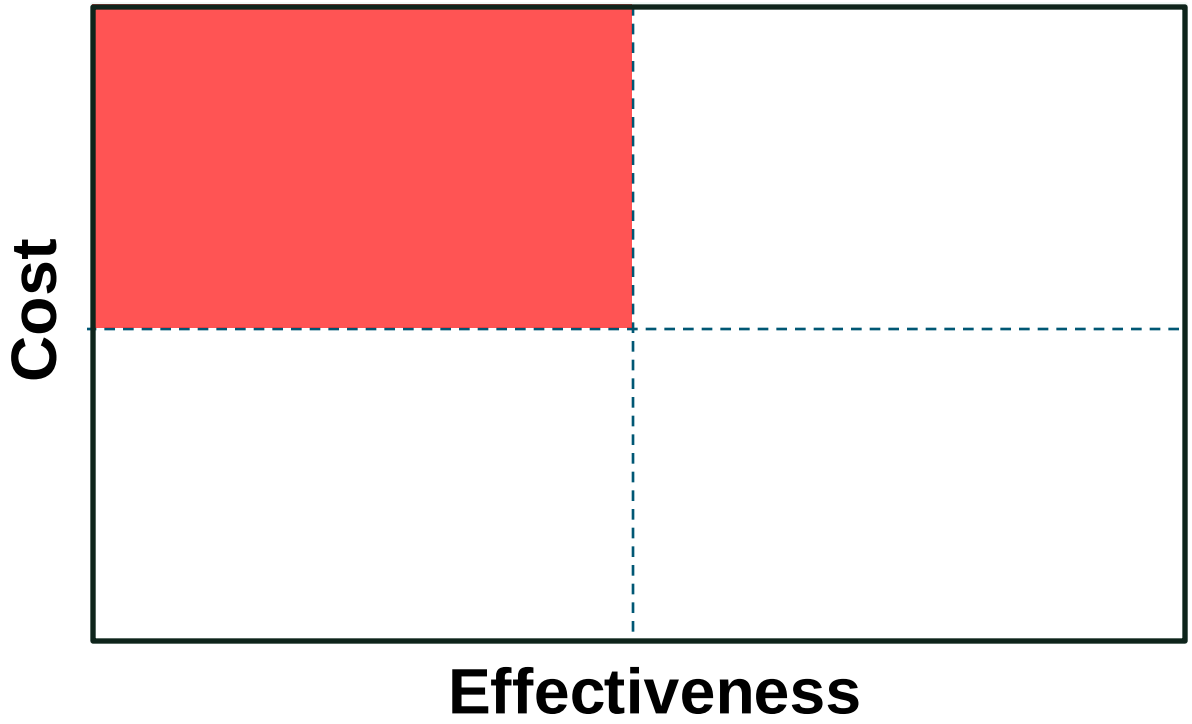

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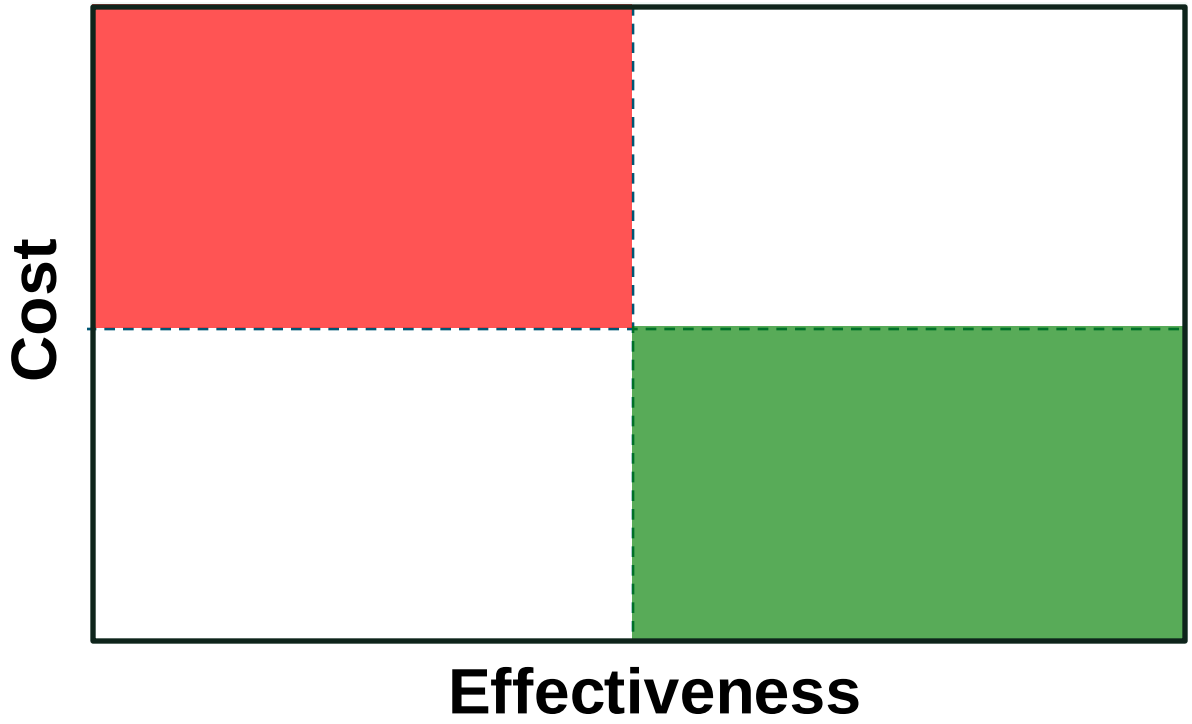

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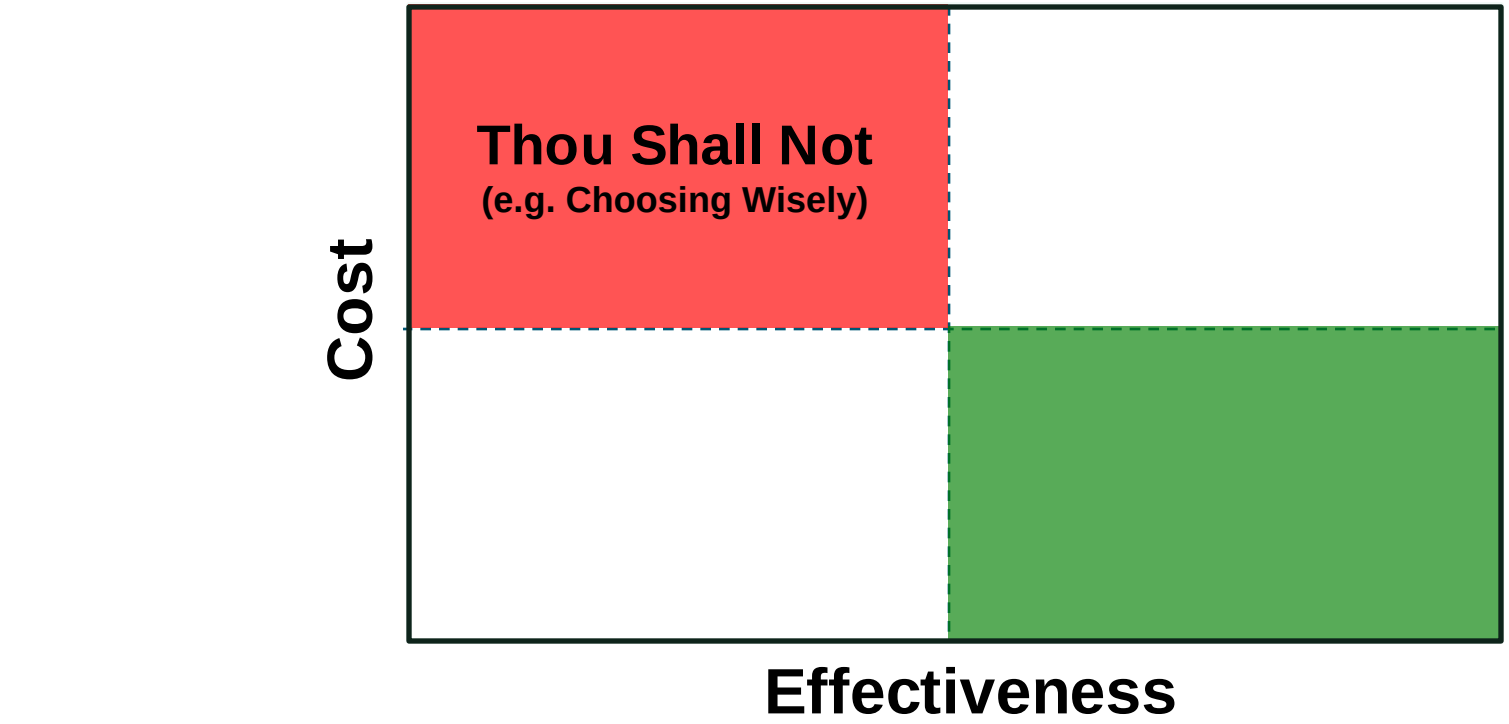

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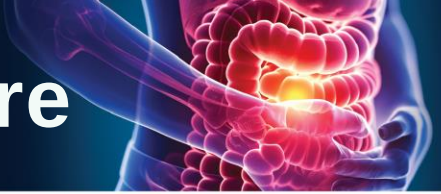

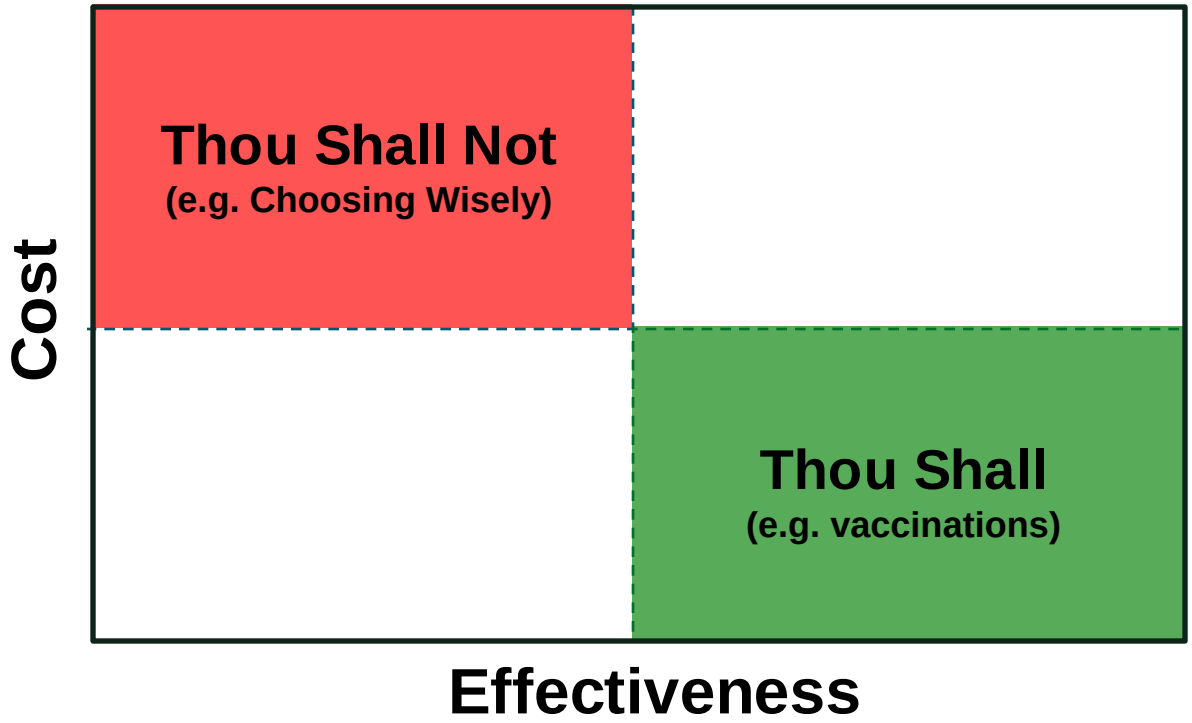

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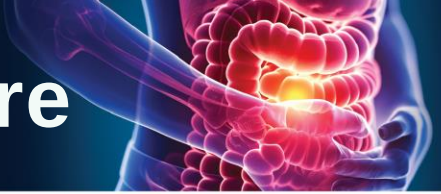

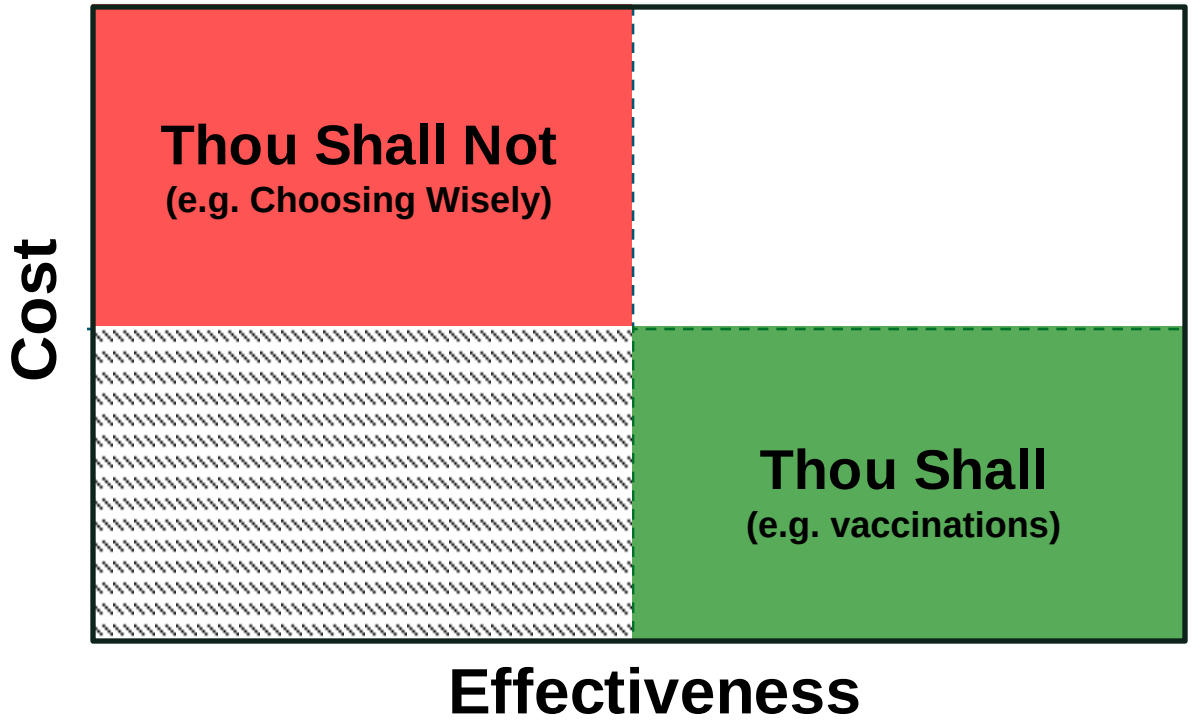

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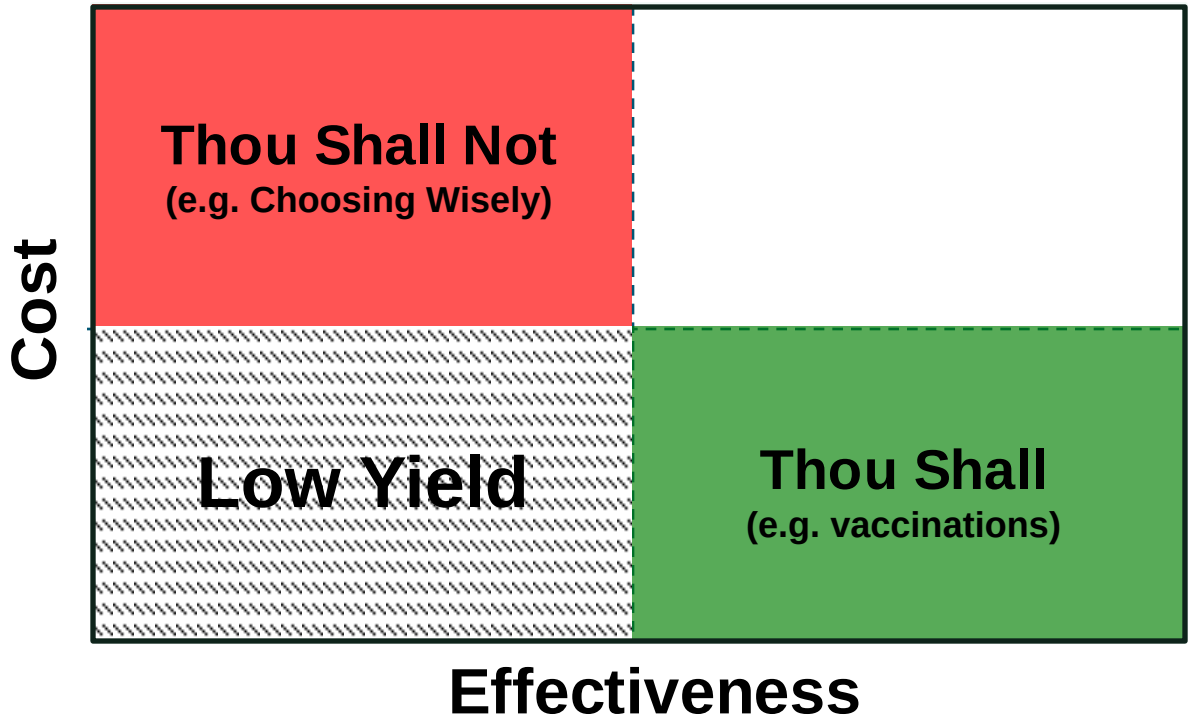

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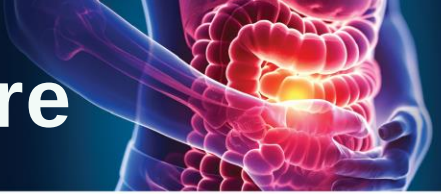

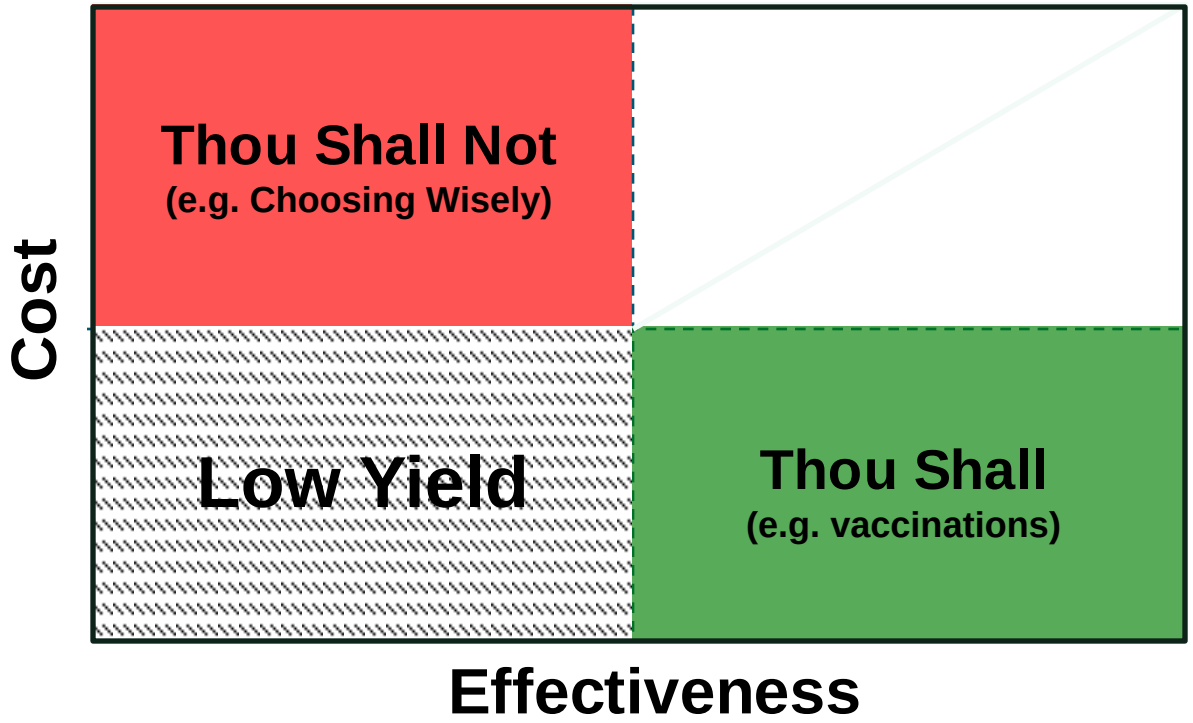

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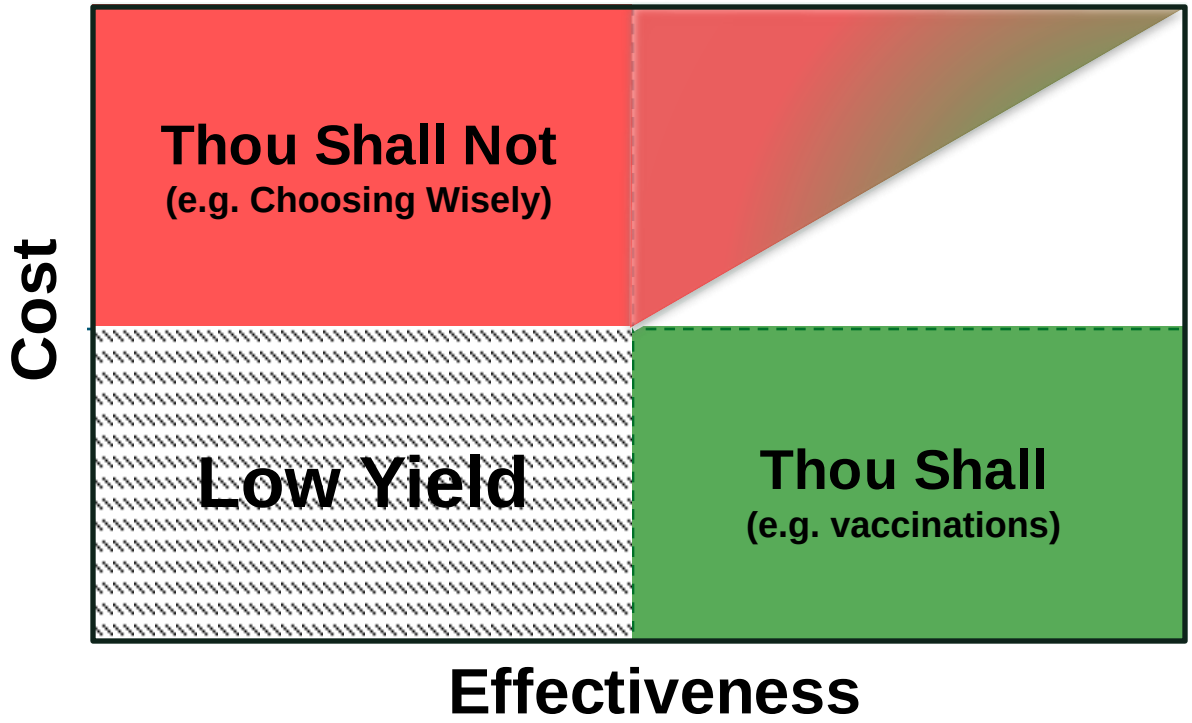

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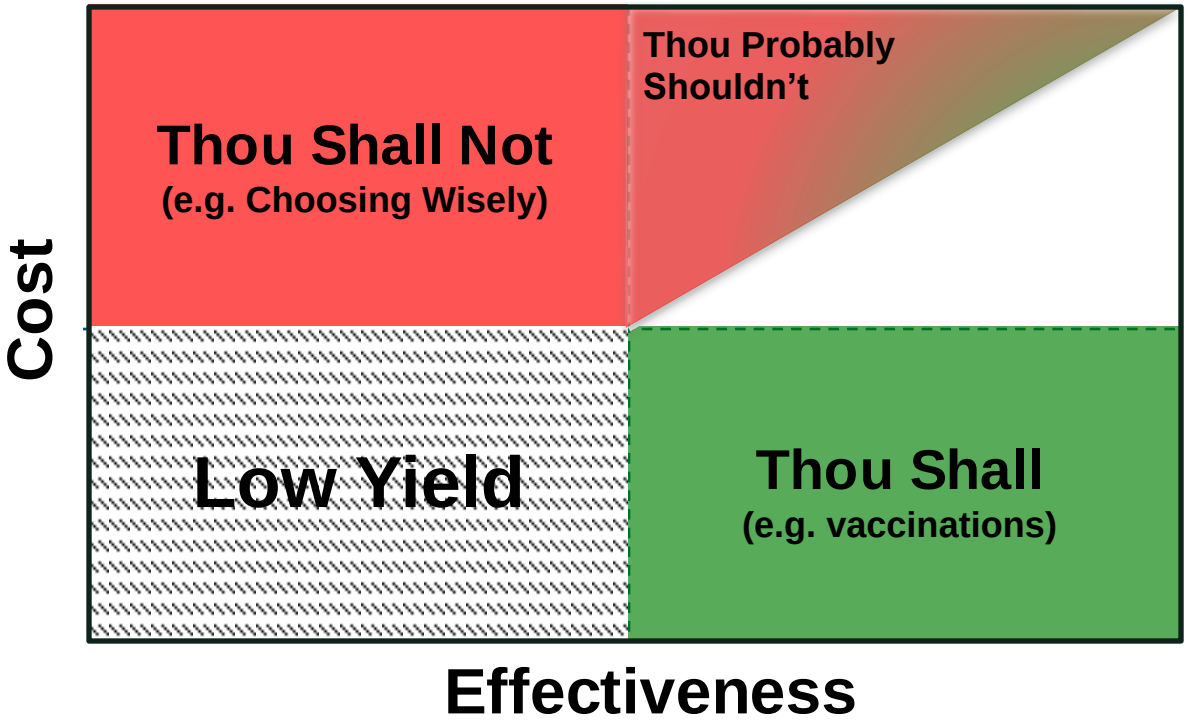

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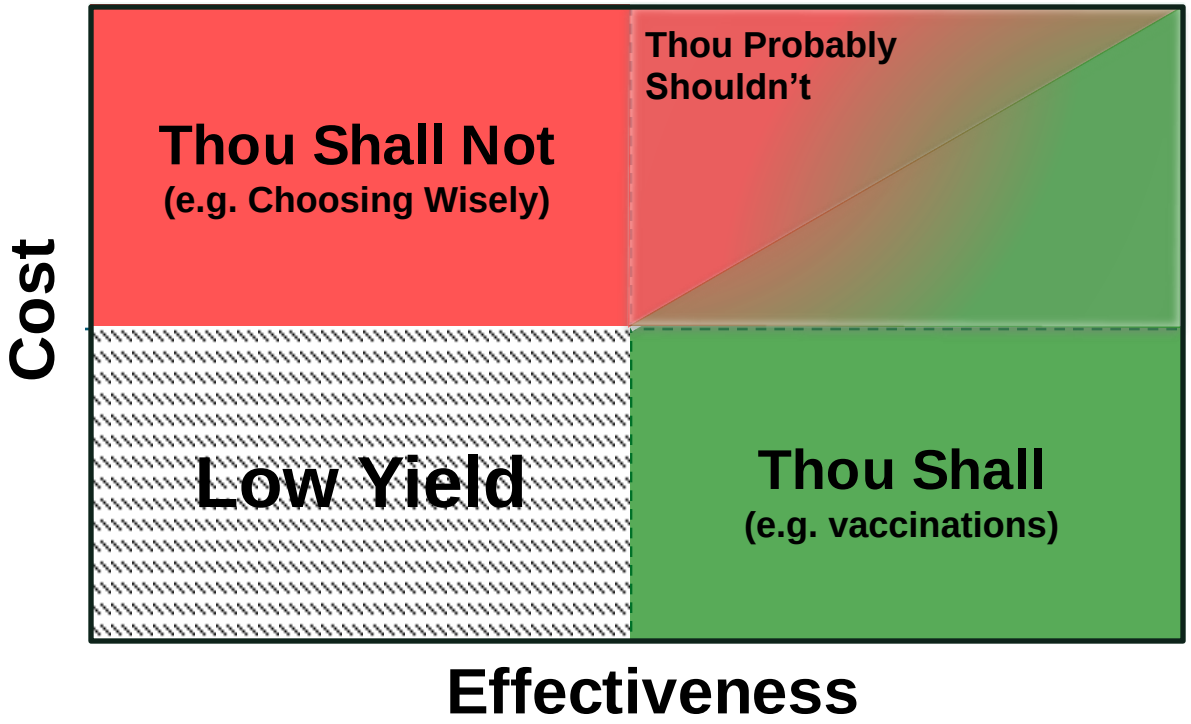

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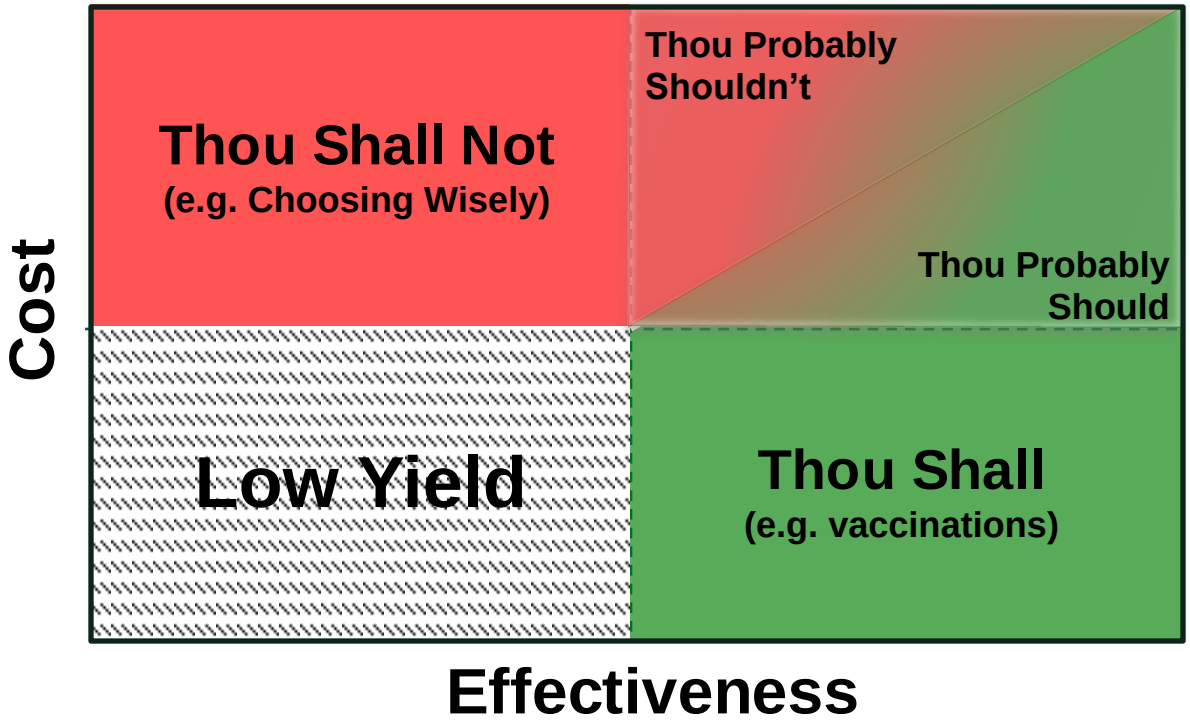
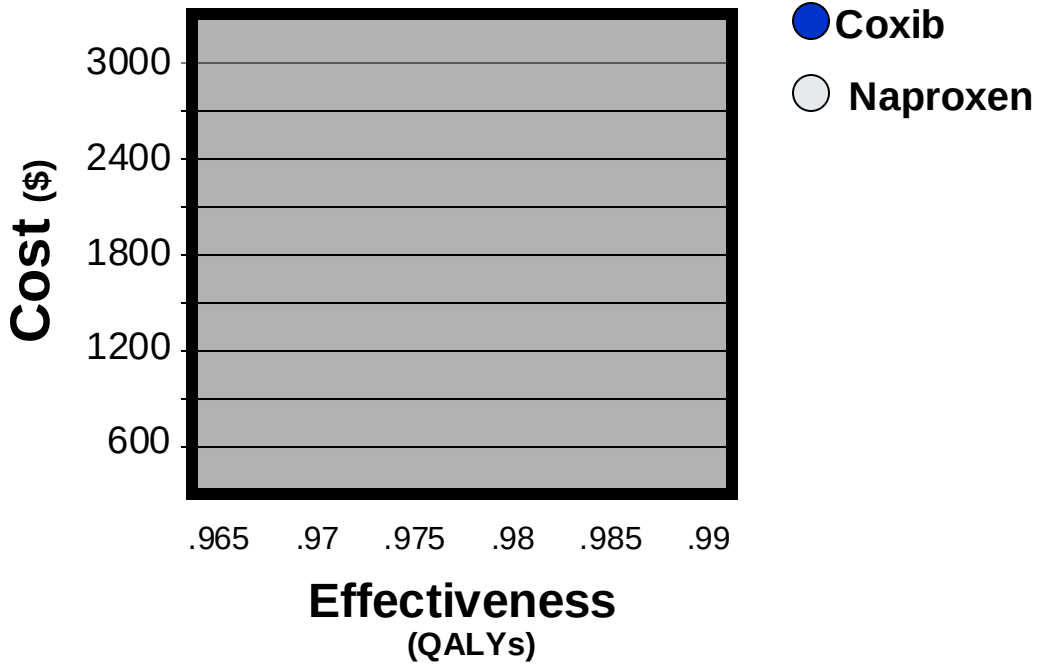


The Cost-Effectiveness Plane



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Lester et al. *CMAJ Open* 2021

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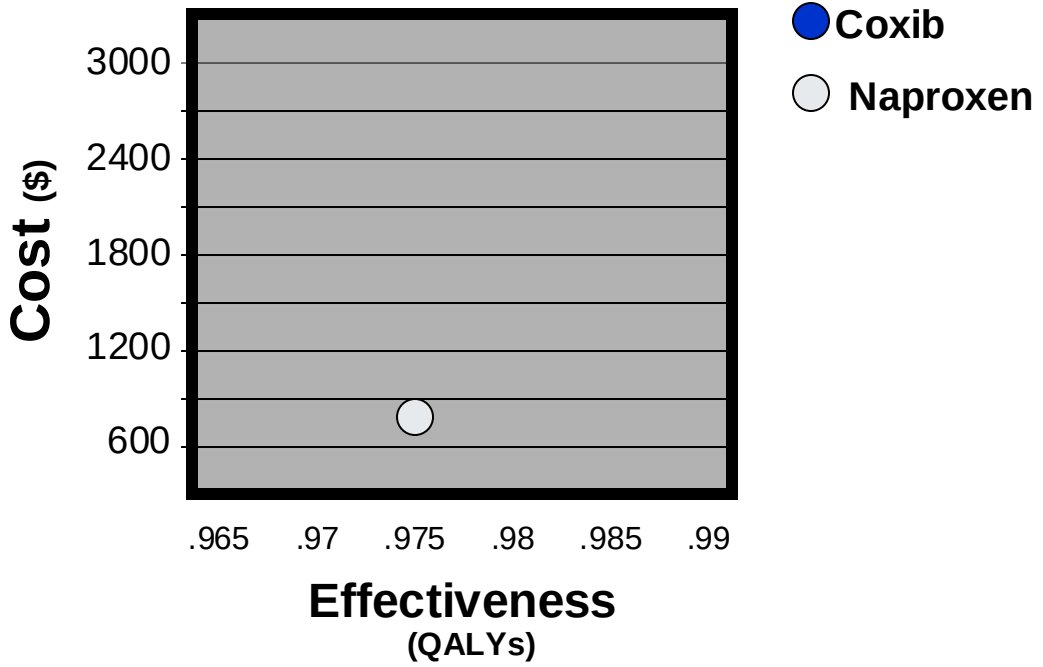

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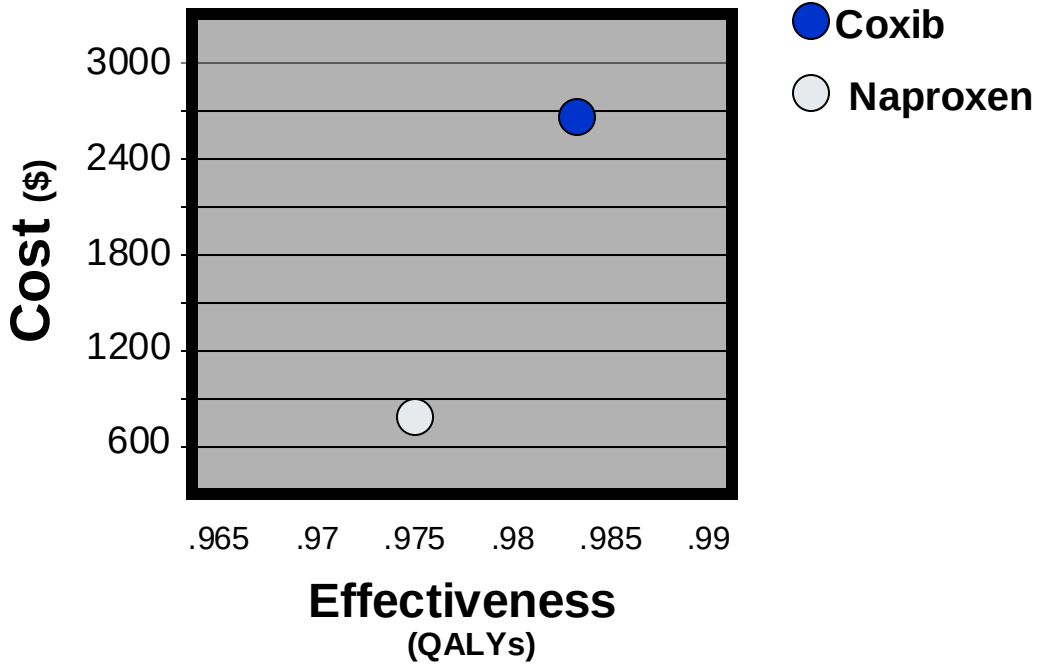

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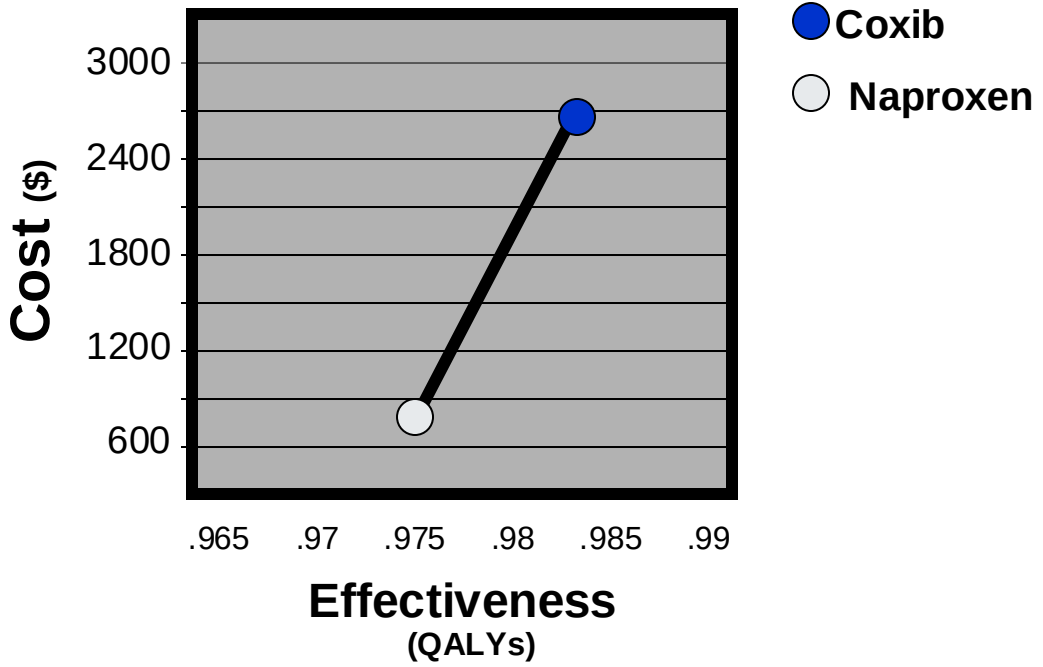

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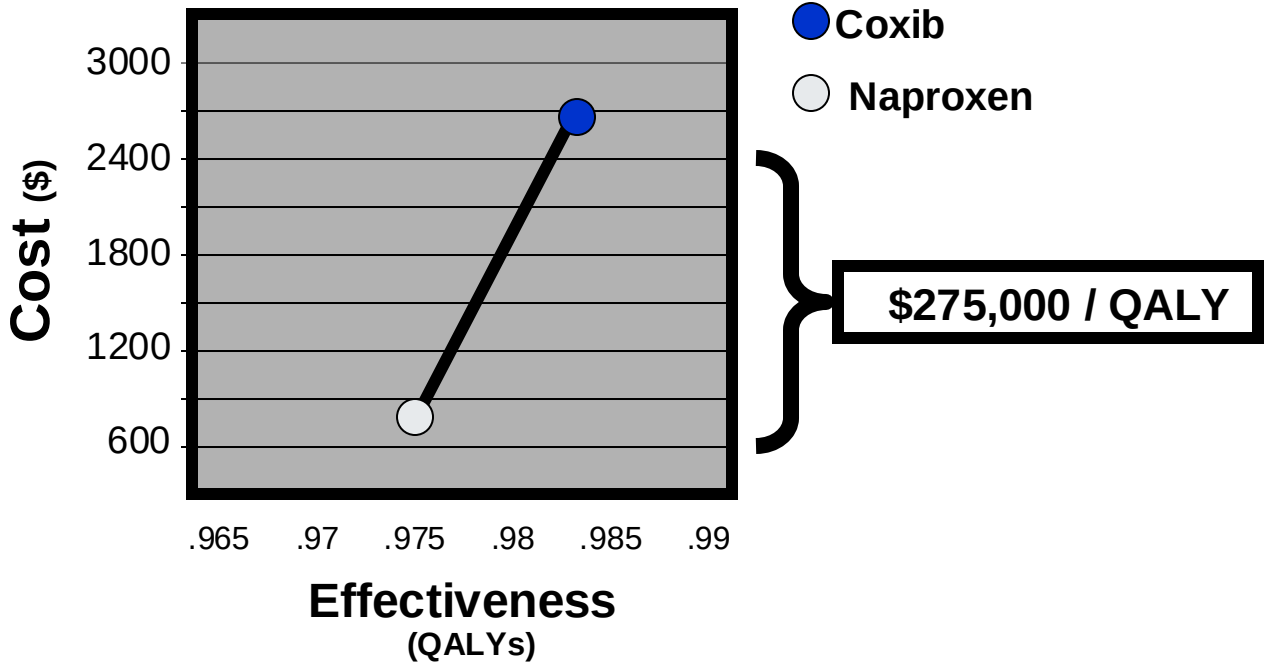

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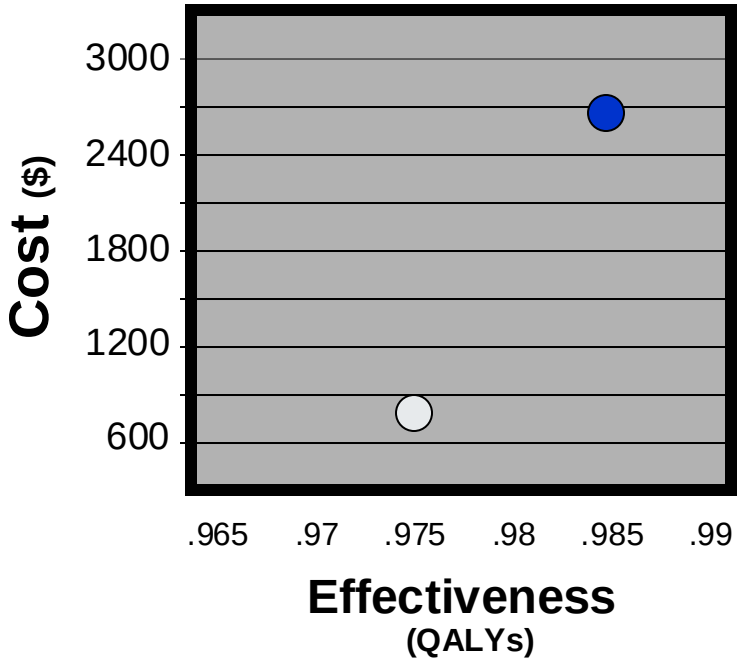

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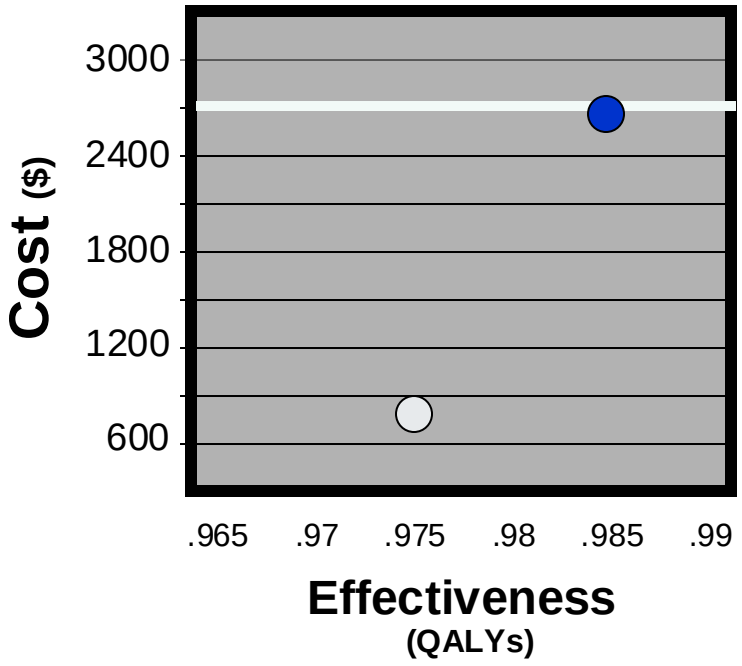

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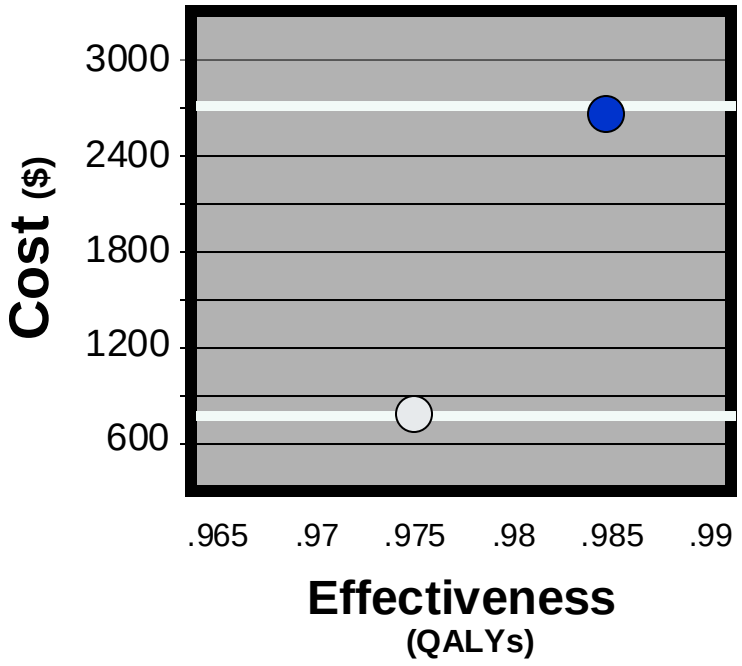

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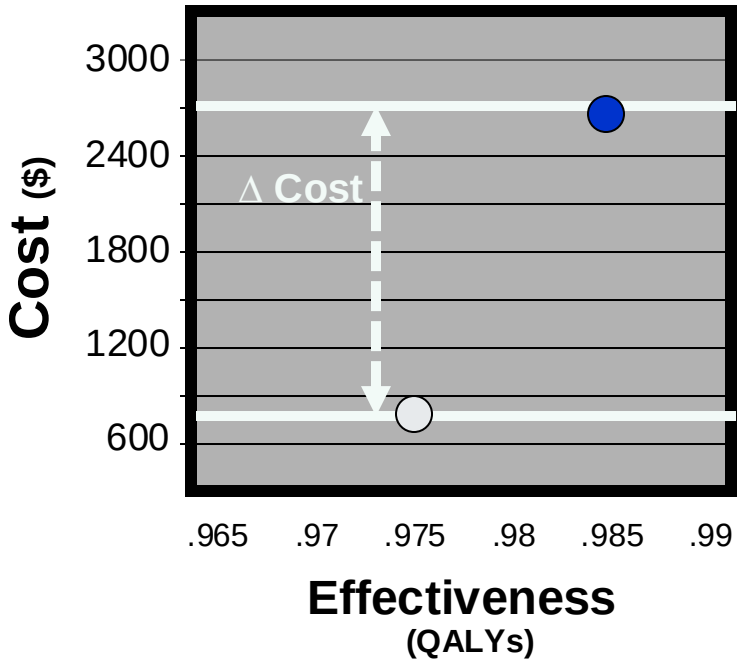

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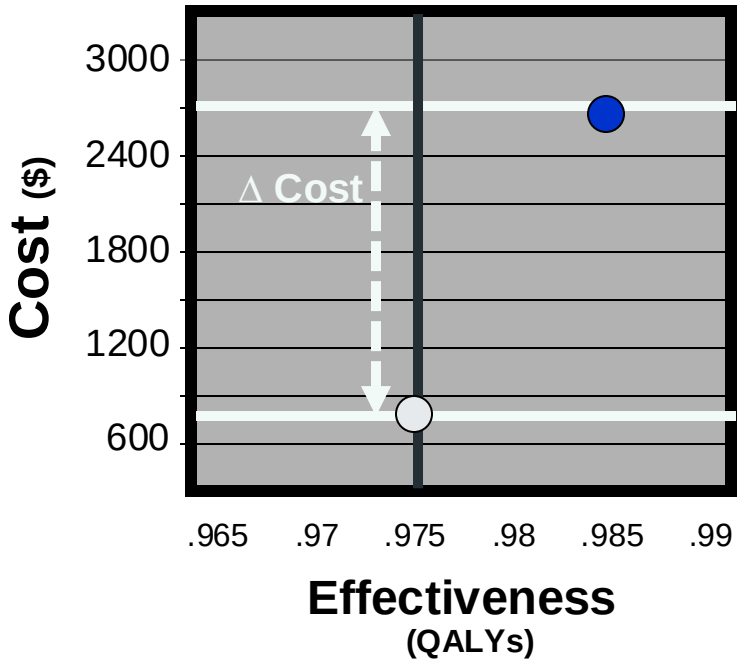

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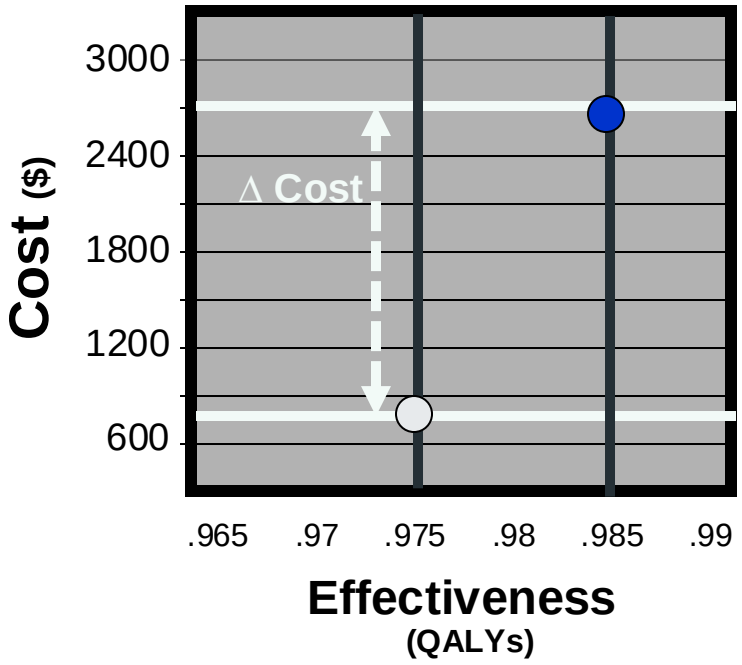
Lester et al. *CMAJ Open* 2021

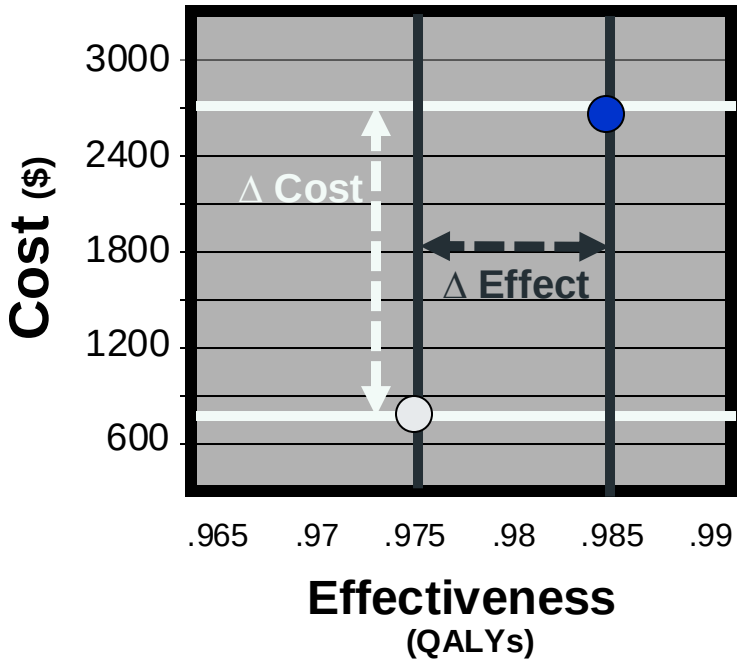
The Cost-Effectiveness Plane



Spiegel BMR, et al. *Ann Intern Med.* 2003;138:795-806.

Lester et al. *CMAJ Open* 2021

The Cost-Effectiveness Plane



Spiegel BMR, et al. *Ann Intern Med.* 2003;138:795-806.

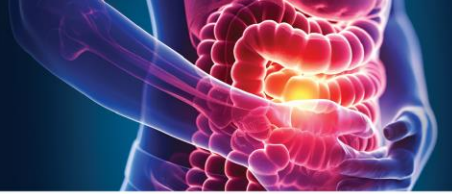
Lester et al. *CMAJ Open* 2021

Is the Juice Worth the Squeeze?

$$\text{ICER} = \frac{\Delta \text{ Cost}}{\Delta \text{ Effect}}$$

ICER = incremental cost-effectiveness ratio

ICERs of Biologics for IBD



RESEARCH ARTICLE

A Systematic Review of the Cost-Effectiveness of Biologics for the Treatment of Inflammatory Bowel Diseases

Saara Huoponen*, Marja Blom

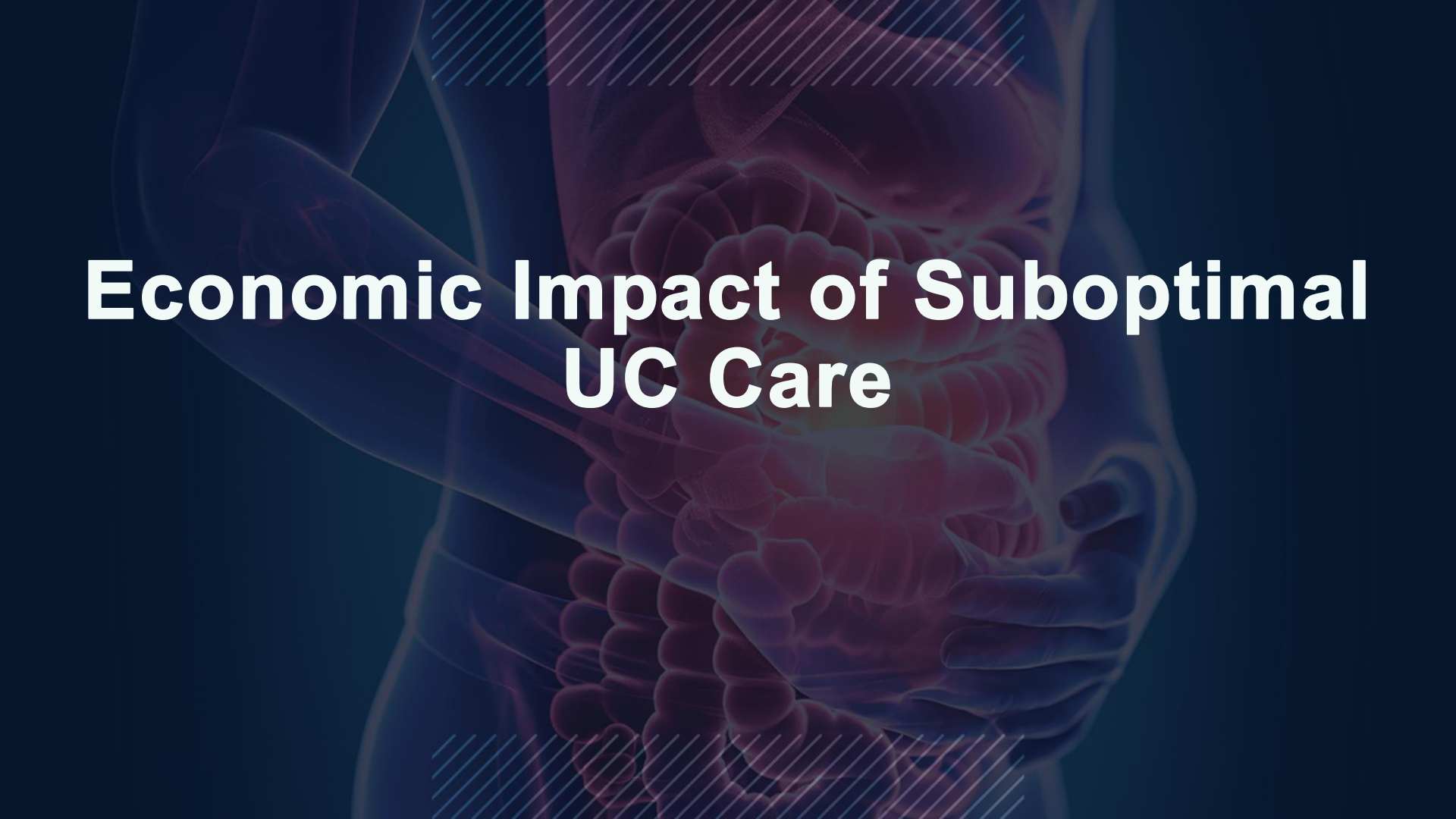
Conclusions

With a threshold of 35,000 €/Quality-Adjusted Life Year, biologics seem to be cost-effective for the induction treatment of active and severe inflammatory bowel disease. Between biologics, the cost-effectiveness remains unclear.

Huoponen S, Blom M. *PLoS One.* 2015 Dec 16;10(12):e0145087.

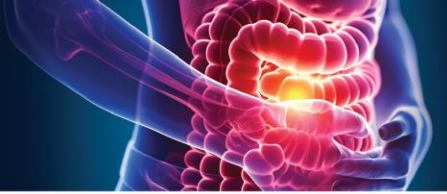
Unmet Needs

- More budget impact models
- Tailored models to individual healthcare systems
- Optimizing AI to identify highest impact prescribing
- More comparative effectiveness data
- Active involvement of patients and providers in designing models and discussing with payors



Economic Impact of Suboptimal UC Care

Audience Response

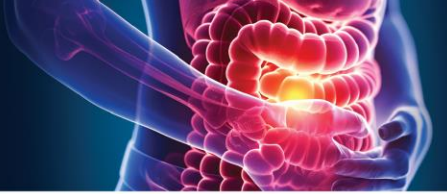


Failure on an ulcerative colitis treatment results in an annual increase in cost of care by what amount?

A. $10,000
B. $18,000
C. $23,000
D. $29,000
E. I don’t know

CME OUTFITTERS

Audience Response



Failure on an ulcerative colitis treatment results in an annual increase in cost of care by what amount?

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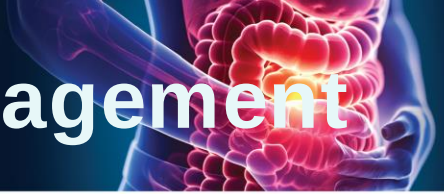
CME OUTFITTERS

Economic Challenges in UC Management



- Ulcerative colitis has a high cost of care
- Disease symptoms and/or progression results in hospitalization, steroid dependence, and surgery
- Treatments often fail or result in inadequate response
- Adverse event management increases healthcare resource utilization
- Switching therapy to improve response is common
- Dosing changes add cost burden
  - Increase to obtain a response
  - Decrease to manage adverse events

Pilon D, et al. *Curr Med Res Opinion.* 2020;36(8):1285-1294.

Costs of UC Treatment

Average Annual Cost for Advanced Therapy[1]
$42,579

Cost of Adverse Events[2]
Serious AEs:
$7,060
Serious Infections:
$10,774

Average Cost of Surgical Care[3]
$40,300

1. Long MD, et al. *Inflamm Bowel Dis.* 2020;26(6):941-948. 2. Jairaath V, et al. *BMC Gastroenterol.* 2020;22:501. 3. Ng AP, et al. *J Gastrointest Surg.* 2024;28(4):488-493.

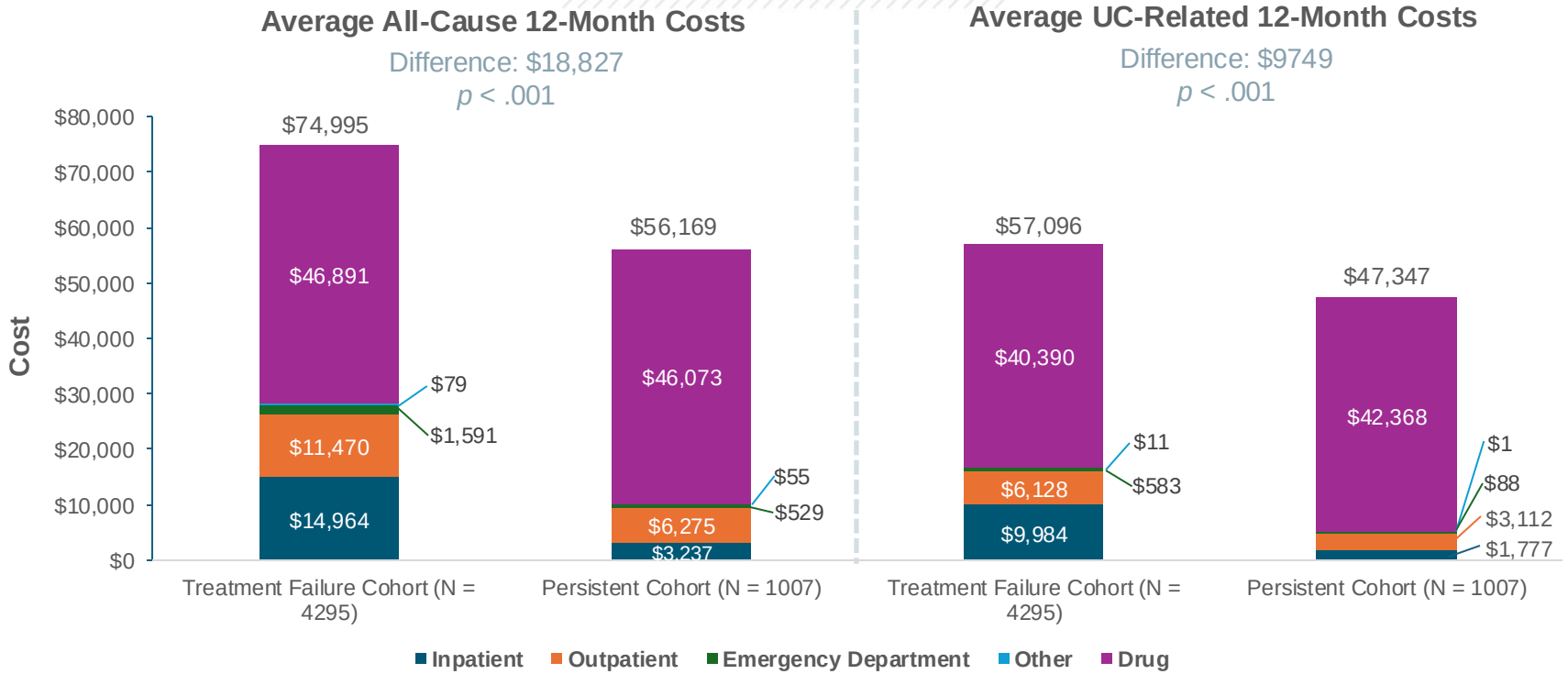
Impact of Biologic Therapy on Overall Cost of Care

Infliximab Treatment, 2015 Costs

	Prior to Treatment	1-Year Follow Up
Inpatient hospitalization, n (%)	504 (33.8%)	172 (11.5%)
Cost per patient	$9777	$3283.48
Emergency department visit, n (%)	638 (42.8%)	381 (25.6%)
Cost per patient	$1400	$764
Outpatient visit, n(%)	1483 (99.6%)	1486 (99.8%)
Pharmacy cost per patient	$6214	$45710

Perera S, et al. *J Health Con Outcomes Res.* 2018;6(1):96-112.

Cost of Treatment Failure



Lee SD, et al. *Crohns Colitis 360*. 2024;6(2):otae026.

Cost of Care for Patients

- Crohn's & Colitis Foundation's Cost of IBD Care Initiative
- Patients with IBD have significantly higher healthcare costs compared to individuals without IBD
  - 3x increase in direct care costs
  - 2x increase in out-of-pocket costs
  - Average cost burden in first year following diagnosis: $26,555

Park KT, et al. *Inflamm Bowel Dis.* 2020;26(1):1-10.

Dealing with insurance denials

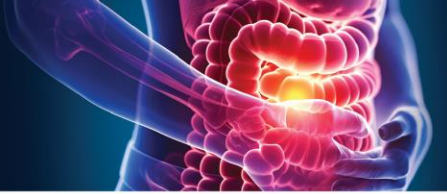
Faculty Discussion

Costs of active UC and disease monitoring and management

Faculty Discussion

Integrating Novel Therapies for UC in Population Health Decisions

Audience Response



Which of the following ulcerative colitis treatments is only approved for use in patients who are resistant or intolerant to TNF inhibitors?

A. Upadacitinib
B. Ozanimod
C. Guselkumab
D. Vedolizumab
E. I don’t know

CME OUTFITTERS

Treatment Challenges in UC

- Patients often require therapy changes before achieving remission
- Resistance to standard therapies like TNF inhibitors
- Limited treatment options beyond TNF inhibitors
- Side effect profiles of advanced therapies
- Patient reluctance to try advanced therapies
- Majority of uninsured patients cannot afford the cost of treatment

Fukuda T, et al. *Intest Res.* 2019;17(1):36-44.

Treatment Targets for Advanced UC: STRIDE II

Treatment target	Definition
Clinical response	≥ 50% decrease in baseline Patient Reported Outcomes 2 (PRO2) (rectal bleeding and stool frequency)
Clinical remission	PRO2 with rectal bleeding = 0 and stool frequency score = 0; or partial Mayo (< 3 and no score >1).
Patient reported outcomes	Clinical outcomes evaluated using PRO2; absence of disability and normalization of health-related quality of life
Biomarker normalization	C-reactive protein < upper limit of normal; fecal calprotectin normalization
Endoscopic healing	Mayo endoscopic subscore = 0 points, or UCEIS ≤1 points

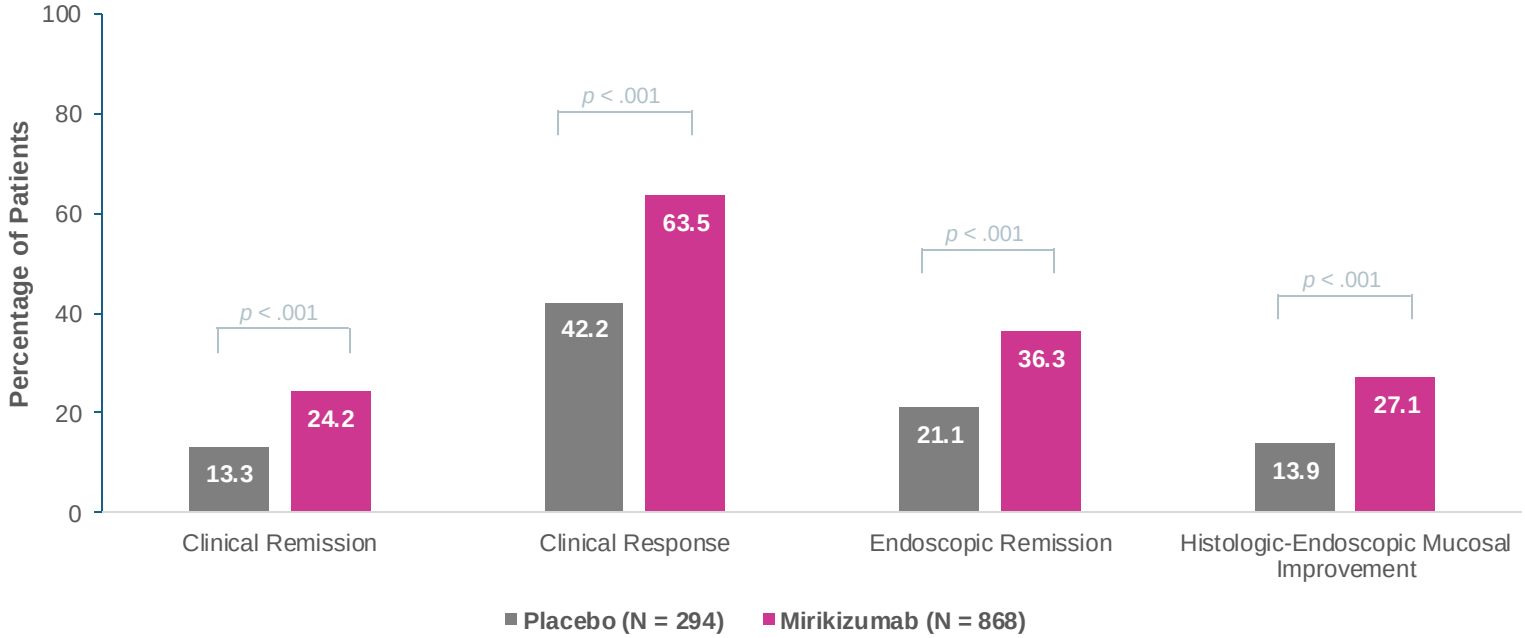
Turner D. et al. *Gastroenterology.* 2021 Apr;160(5):1570-1583.

New Treatments for Moderate to Severe UC Approved Since 2020

Treatment	Target	Year Approved	Indication
Ozanimod	S1P receptor	2021	Adults with moderately to severely active UC
Upadacitinib	JAK1/2	2022	Moderately to severely active UC in adults who have had inadequate response or intolerance to one or more TNF blockers
Mirikizumab	IL-23	2023	Adults with moderately to severely active UC
Etrasimod	S1P receptor	2023	Adults with moderately to severely active UC
Guselkumab	IL-23	2024	Adults with moderately to severely active UC
Risankizumab	IL-23	2024	Adults with moderately to severely active UC

Ozanimod [package insert]. https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/209899s005lbl.pdf.;
Upadacitinib [package insert]. https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/211675s015lbl.pdf;
Mirikizumab [package insert]. https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/761279s000lbl.pdf;
Etrasimod [package insert]. https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/216956s000lbl.pdf; Brooks A. HCPLive. 2024. https://www.hcplive.com/view/fda-approves-guselkumab-tremfya-for-ulcerative-colitis;
Risankizumab [package insert]. https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/761105s029,761262s007lbl.pdf

Mirikizumab in UC Induction: LUCENT-1



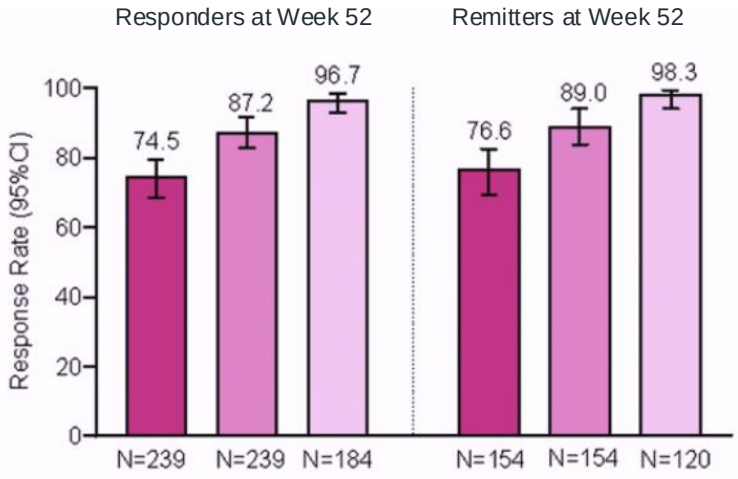
Mirikizumab is indicated for the treatment of moderately to severely active ulcerative colitis in adult patients.

D'Haens G, et al. *N Engl J Med*. 2023;388:2444-2455.

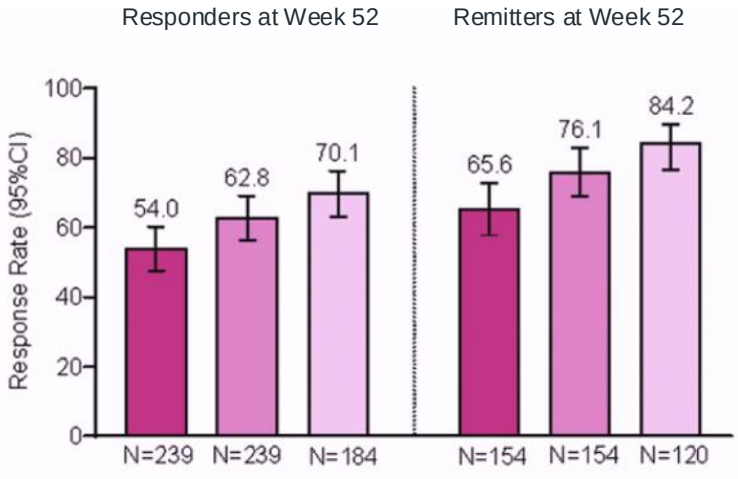
CME OUTFITTERS

Mirikizumab Long-Term Follow-Up in UC

Clinical Response at Week 104



Clinical Remission at Week 104



NRI **Modified NRI** **Observed case**

NRI = nonresponder imputation

Mirikizumab is indicated for the treatment of moderately to severely active ulcerative colitis in adult patients.

Sands BE, et al. *Inflamm Bowel Dis*. 2024 Mar 9:izae024. [Epub ahead of print.]

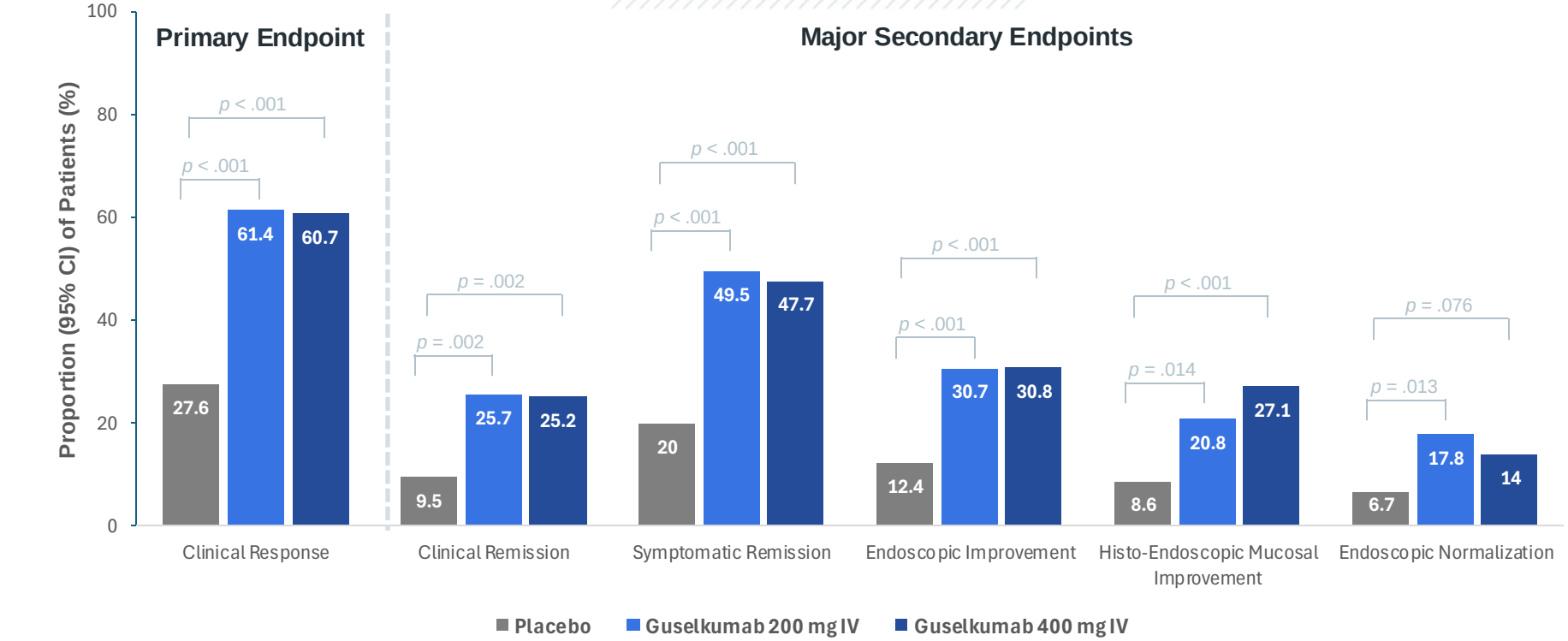
CME OUTFITTERS

Mirikizumab Safety in UC

Outcome, n (%)	200 mg mirikizumab Q4W SC (n = 289)
TEAEs	184 (63.7)
AEs of Special Interest	
Infections (all)	87 (30.1)
Infections (serious)	3 (1.0)
Cerebrocardiovascular events	2 (0.7)
Malignancies	0 (0)
Immediate hypersensitivity reaction	4 (1.4)
Injection site reactions	16 (5.5)
Death	0 (0)
Discontinuation due to AE	8 (2.8)

Sands BE, et al. *Inflamm Bowel Dis*. 2024 Mar 9:izae024. [Epub ahead of print.]

Guselkumab in UC Induction: QUASAR 12 Week Endpoints



Guselkumab is indicated for adult patients with moderately to severely active ulcerative colitis.

Peyrin-Biroulet L, et al. *Gastroenterology*. 2023;165:1443-1457.

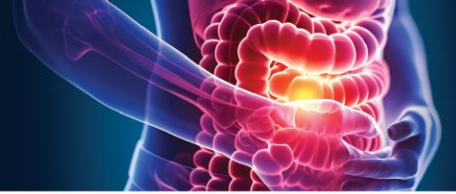
CME OUTFITTERS

Guselkumab Safety in UC

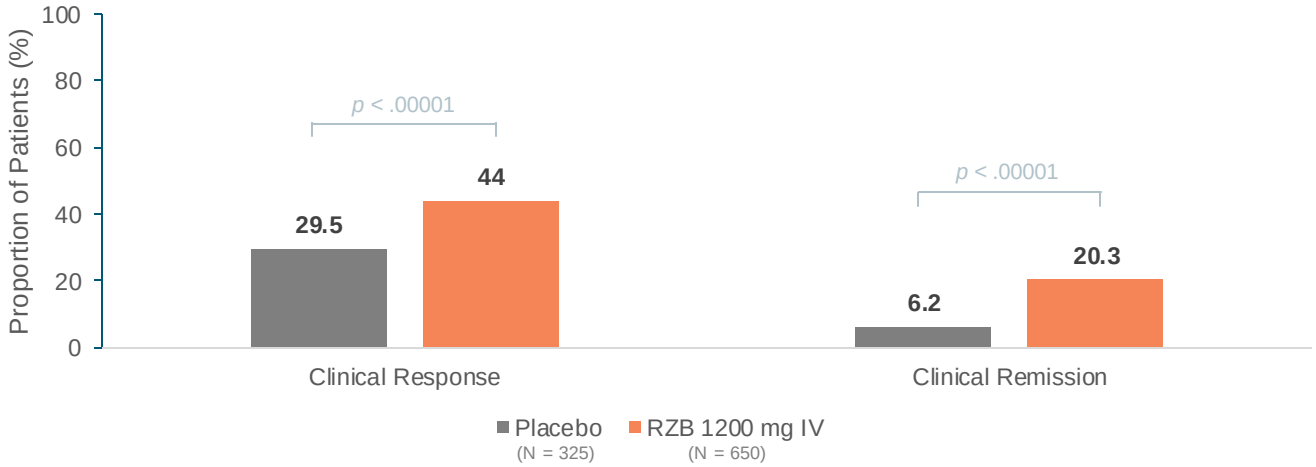
Outcome	Placebo (n = 105)	Guselkumab 200 mg IV (n = 101)	Guselkumab 400 mg IV (n = 107)	Combined (n = 208)
Any AE	59 (56.2)	45 (44.6)	53 (49.5)	98 (47.1)
AE within 1 hour of infusion	2 (1.9)	2 (2.0)	0	2 (1.0)
Serious AE	6 (5.7)	1 (1.0)	3 (2.8)	4 (1.9)
Death	0	0	0	0
Discontinuation for AE	3 (2.9)	1 (1.0)	0	1 (0.5)
Malignancy	0	0	0	0
Infection	13 (12.4)	14 (13.9)	10 (9.3)	24 (11.5)
Serious Infection	2 (1.9)	0	0	0

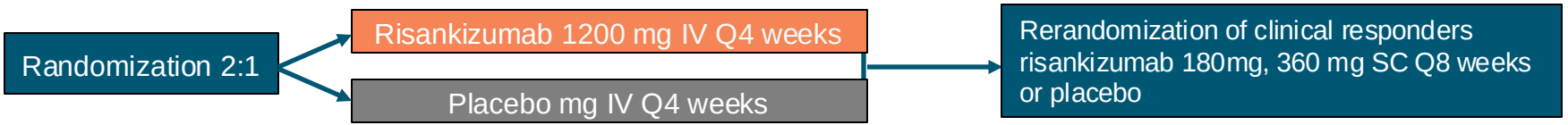
Peyrin-Biroulet L, et al. *Gastroenterology* 2023;165(6):1443-1457.

Risankizumab Induction in UC: INSPIRE



Clinical Response and Remission at 12 Weeks





Risankizumab is indicated for adults with moderately to severely active UC.

Clinical responders defined as ≥30% decrease in average daily stool frequency or APS and not worse than baseline; *Endoscopic response defined as >50% decline in SES-CD vs BL by central reviewer (or in pts with SES-CD of 4 at BL, ≥2-point decrease vs BL); CDAI clinical remission a CDAI < 150.

Louis E, et al. *Am J Gastroenterol*. 2023;118(10S):S624-S625.

CME OUTFITTERS

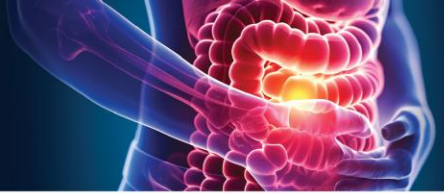
Rizankizumab Safety in UC

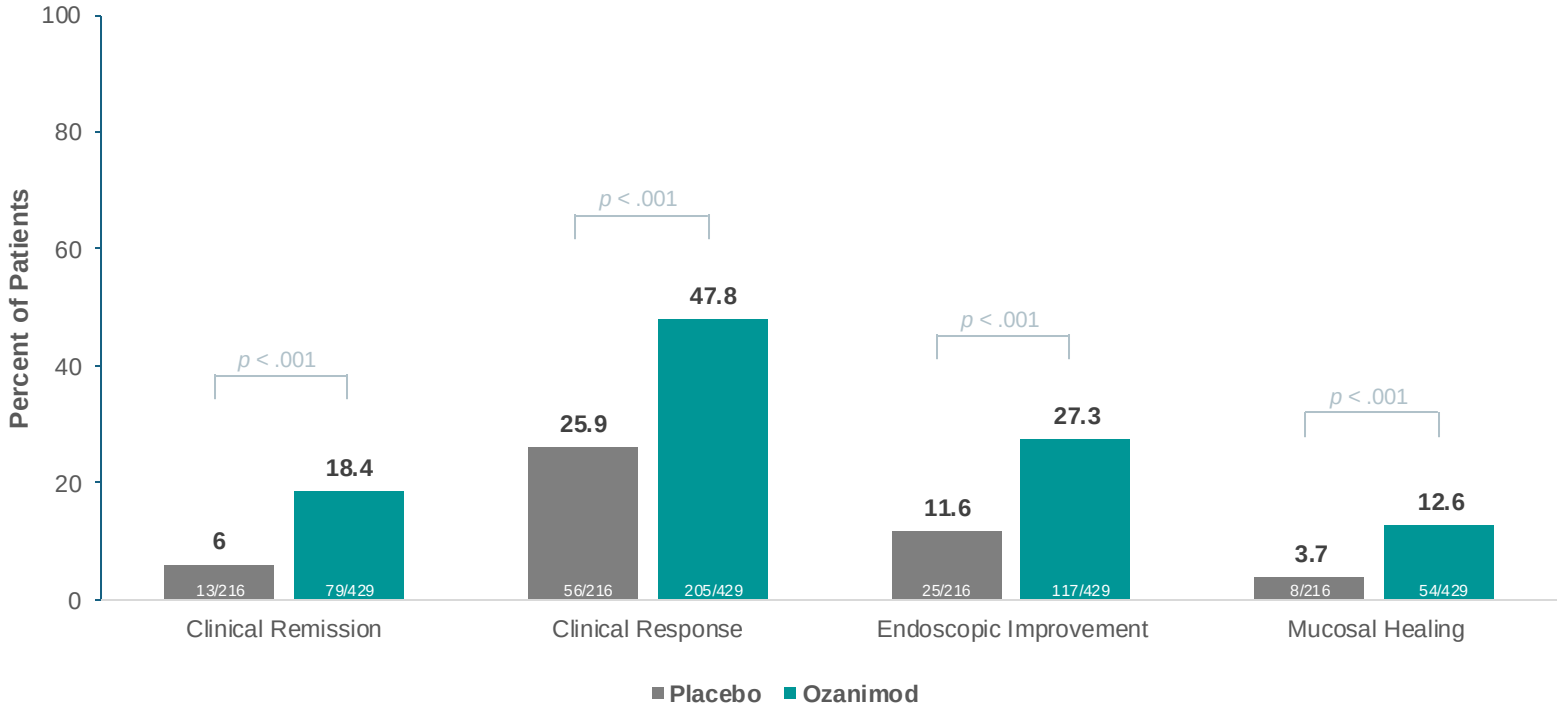
Treatment-Emergent Adverse Events Among Safety Population Through Week 52[a]			
E/100 PY	**PBO (WD) SC n = 196; PY = 174.9**	**RZB 180 mg SC n = 193; PY = 185.4**	**RZB 360 mg SC n = 195; PY = 173.5**
Any AE:	399 (228.1)	399 (215.2)	406 (234.0)
AE related to COVID-19	28 (16.0)	21 (11.3)	29 (16.7)
AE with reasonable possibility of being drug-related[b]	75 (42.9)	85 (45.9)	61 (35.2)
Severe AE	14 (8.0)	3 (1.6)	7 (4.0)
Serious AE	20 (11.4)	11 (5.9)	11 (6.3)
AE leading to discontinuation of study drug	4 (2.3)	5 (2.7)	5 (2.9)
All deaths	0	0	1 (0.6)[c]
Serious infections[d]	4 (2.3)	2 (1.1)	1 (0.6)
Infusion/Injection site reactions[e]	3 (1.7)	14 (7.6)	10 (5.8)

AE = adverse event; COVID-19 = coronavirus disease 2019; E = events; patient-years; PBO = placebo; RZB = risankizumab; SC = subcutaneous; WD = withdrawal. [a]The safety population included all patients who clinically responded to IV RZB at 12 or 24 weeks, were randomised to COMMAND at maintenance week O, and received at least one dose of study drug during 52-week maintenance period. [b]As assessed by the investigator. [c]One death was reported in the RZB360 arm in a patient diagnosed with colon adenocarcinoma, which was retrospectively found in the screening biopsy tissue. [d]Serious infections in risankizumab-treated patients included COVID-19, COVID-19 pneumonia, abscess limb, and pneumonia. [e]All infusion/injection site reaction events were nonserious and did not lead to study discontinuation.

Louis E, et al. *J Crohns Colitis.* 2024;18(S1):i10-i12.

Ozanimod in UC Induction: True North, Week 12 Endpoints



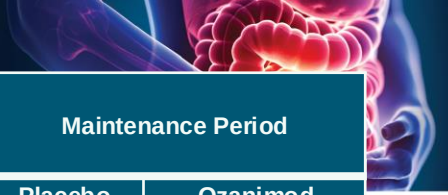


Ozanimod is indicated for adults with moderately to severely active UC

Sandborn WJ, et al. *N Engl J Med.* 2021;385:1280-1291.

CME OUTFITTERS

Ozanimod Safety in UC: True North Study



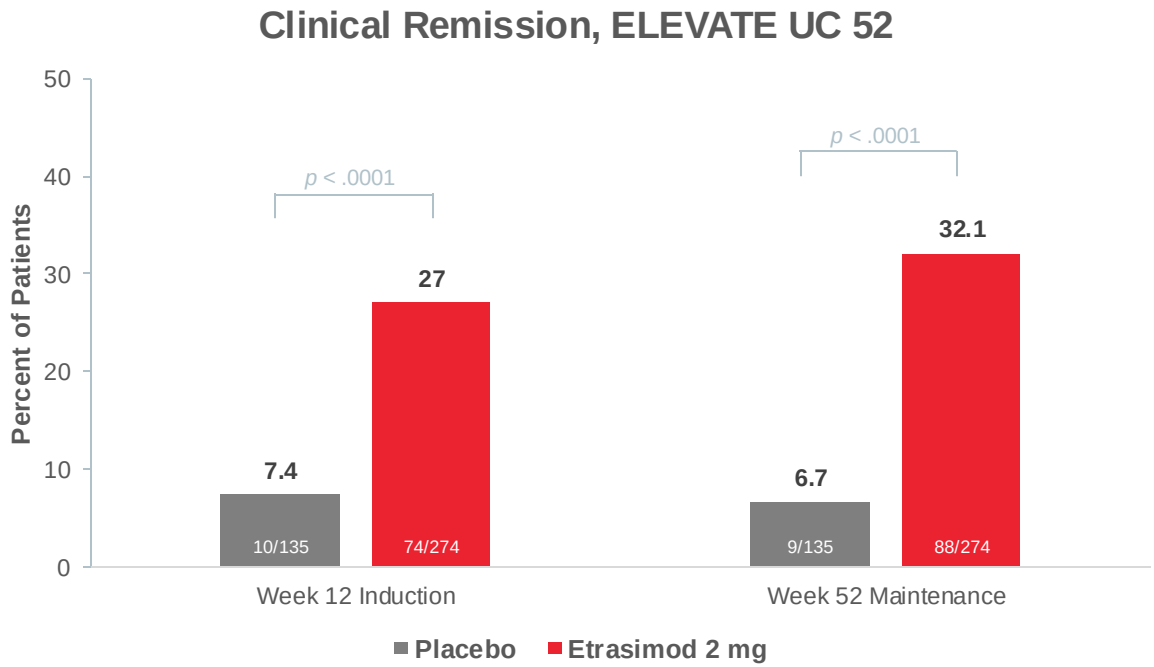
	Induction Period			Maintenance Period	
	Cohort 1		Cohort 2		
	Placebo (n = 216)	Ozanimod (n = 429)	Ozanimod (n = 367)	Placebo (n = 227)	Ozanimod (n = 230)
Any AE – n (%)	82 (38.0)	172 (40.1)	146 (39.8)	83 (36.6)	113 (49.1)
SAEs – n (%)	7 (3.2)	17 (4.0)	23 (6.3)	18 (7.9)	12 (5.2)
AEs leading to discontinuation	7 (3.2)	14 (3.3)	14 (3.8)	6 (2.6)	3 (1.3)
Common AEs (≥ 3% during either period) – n (%)					
Anemia	12 (5.6)	18 (4.2)	16 (4.4)	4 (1.8)	3 (1.3)
Nasopharyngitis	3 (1.4)	15 (3.5)	10 (2.7)	4 (1.8)	7 (3.0)
Headache	4 (1.9)	14 (3.3)	10 (2.7)	1 (0.4)	8 (3.5)
ALT increased	0	11 (2.6)	6 (1.6)	1 (0.4)	11 (4.8)
Arthralgia	3 (1.4)	10 (2.3)	5 (1.4)	6 (2.6)	7 (3.0)
Gamma-glutamyltransferase increased*	0	5 (1.2)	6 (1.6)	1 (0.4)	7 (3.0)
AEs of special interest – n (%)					
Bradycardia	0	2 (0.5)	3 (0.8)	0	0
Hypertension	0	6 (1.4)	7 (1.9)	3 (1.3)	4 (1.7)
Hypertensive crisis	0	1 (0.2)	0	1 (0.4)	1 (0.4)
Macular edema	0	1 (0.2)	1 (0.3)	0	1 (0.4)

*Laboratory values were flagged by the central laboratory if they fell outside the standard reference range. The investigator decided whether the laboratory value qualified as an adverse event.

Ozanimod is indicated for adults with moderately to severely active UC

Sandborn WJ, et al. *N Engl J Med.* 2021;385:1280-1291.

Etrasimod Induction and Maintenance in UC: ELEVATE UC 52



Etrasimod is indicated for adults with moderately to severely active UC

Sandborn WJ, et al. *Lancet.* 2023;401(10383):1159-1171.

CME OUTFITTERS

Etrasimod Safety: ELEVATE UC Studies

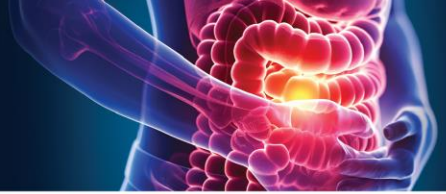
	ELEVATE UC 52		ELEVATE UC 12	
	Placebo (n = 144)	Etrasimod (n = 289)	Placebo (n = 116)	Etrasimod (n = 238)
Any adverse events	81 (56%)	206 (71%)	54 (47%)	112 (47%)
Any serious adverse events	9 (6%)	20 (7%)	2 (2%)	6 (3%)
Any adverse event leading to study treatment discontinuation	7 (5%)	12 (4%)	1 (1%)	13 (5%)
Adverse events leading to death	0	0	0	0
Adverse events of special interest				
Serious infections	5 (3%)	3 (1%)	0	0
Herpes zoster	0	2 (1%)	2 (2%)	0
Opportunistic infections	1 (1%)	0	0	1 (< 1%)
Hypertension	1 (1%)	8 (3%)	1 (1%)	3 (1%)
Sinus bradycardia	0	0	0	4 (2%)
Bradycardia	0	4 (1%)	0	1 (< 1%)
Atrioventricular block, first degree	0	1 (< 1%)	0	1 (< 1%)
Atrioventricular block, second degree (Mobitz I)	0	1 (< 1%)	0	0

Etrasimod is indicated for adults with moderately to severely active UC

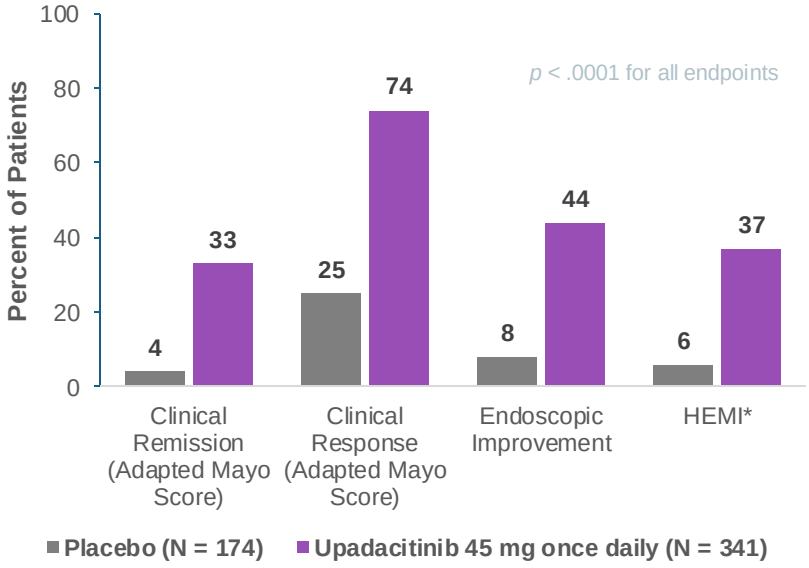
Sandborn WJ, et al. *Lancet.* 2023;401(10383):1159-1171.

CME OUTFITTERS

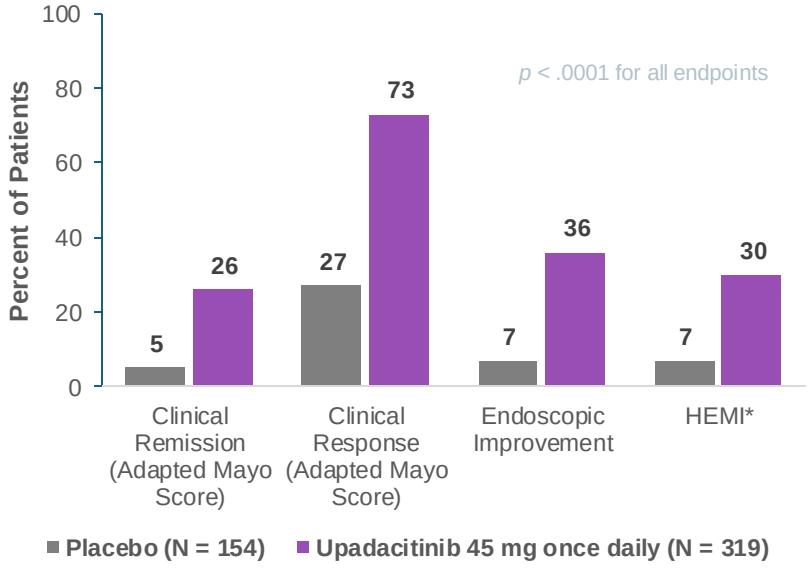
Upadacitinib in UC Induction: Week 8 Endpoints



U-ACCOMPLISH



U-ACHIEVE



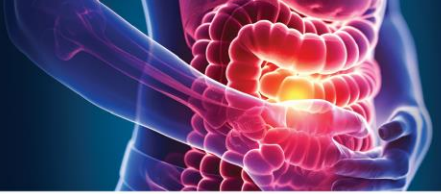
Upadacitinib is indicated for the treatment of moderately to severely active ulcerative colitis in adults who have had inadequate response or intolerance to one or more TNF blockers.

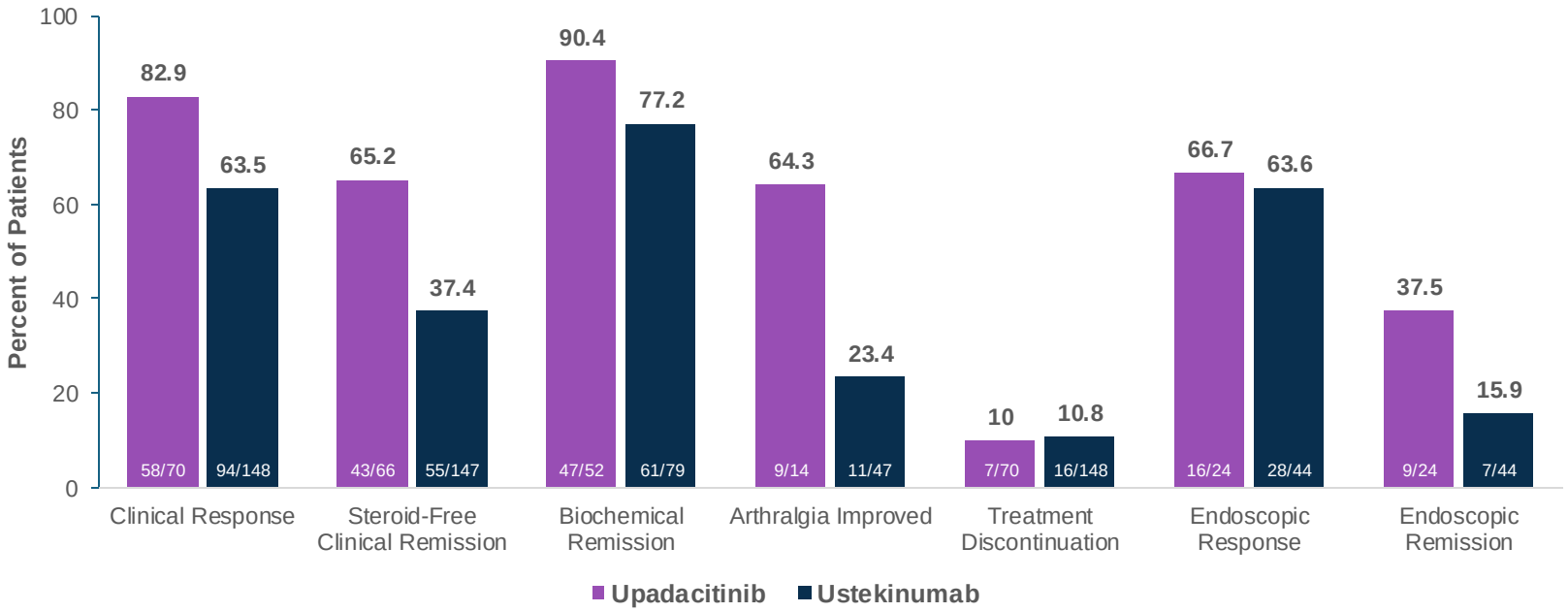
*HEMI defined as an endoscopic subscore of < 1 without friability and Geboes score < 3.1.

Danese S, et al. *Lancet*. 2022;399:2113-2128.

CME OUTFITTERS

Upadacitinib vs Ustekinumab with Prior TNFi Treatment





Upadacitinib is indicated for the treatment of moderately to severely active ulcerative colitis in adults who have had inadequate response or intolerance to one or more TNF blockers. Ustekinumab is indicated for adults with moderately to severely active UC.

Dalal RS, et al. *Clin Gastroenterol Hepatol.* 2024;22(3):666-668.

CME OUTFITTERS

Upadacitinib Safety in UC

Adverse Events of Interest U-ACHIEVE[1]

	Placebo (n=149)	Upadacitinib 15 mg once daily (n=148)	Treatment difference (95% CI)*	Upadacitinib 30 mg once daily (n=154)	Treatment difference (95% CI)*
Serious infection	6 (4%); 6.9	5 (3%); 4.2	-0.7 (-5.3 to 3.8)	4 (3%); 3.0	-1.4 (-5.8 to 3.0)
Opportunistic infection (excluding tuberculosis and herpes zoster)	0	1 (1%); 0.8	0.6 (-1.6 to 2.9)	0	0
Malignancy excluding NMSC‡	1 (<1%); 1.1	1 (<1%); 0.8	0 (-2.7 to 2.6)	2 (1%); 1.5	0.6 (-2.3 to 3.5)
NMSC	0	0	0	2 (1%); 1.5	1.3 (-1.2 to 3.9)
Renal dysfunction	1 (<1%); 1.1	1 (<1%); 0.8	0 (-2.7 to 2.5)	1 (<1%); 0.7	0 (-2.6 to 2.5)
Hepatic disorder	3 (2%); 5.7	10 (7%); 16.8	4.8 (-0.1 to 9.7)	8 (5%); 7.4	3.2 (-1.3 to 7.8)
Adjudicated gastrointestinal perforations‡	1 (1%); 2.3	0	-0.7 (-3.0 to 1.6)	0	-0.7 (-3.0 to 1.6)
Adjudicated MACE‡¶	1 (1%); 1.1	0	-0.7 (-2.9 to 1.6)	0	-0.7 (-2.9 to 1.6)
Adjudicated VTE‖	0	0	0	2 (1%); 1.5	1.3 (-1.2 to 3.9)
Anemia‡	9 (6%); 12.6	7 (5%); 5.9	-1.2 (-6.5 to 4.1)	3 (6%); 8.9	4.5 (0.1 to 8.9)
Lymphopenia‡	2 (1%); 3.4	3 (2%); 2.5	0.7 (-2.7 to 4.1)	3 (2%); 3.0	0.7 (-2.7 to 4.0)

Black Box Warning[2]

Increased risk of serious heart-related events such as heart attack or stroke, cancer, blood clots, and death

*Includes non-treatment-emergent deaths. ‡These events were determined on the basis of external adjudication. ¶MACE is defined as cardiovascular death, nonfatal MI, and nonfatal stroke. ‖VTE is defined as deep vein thrombosis and pulmonary embolism (fatal and nonfatal)

1. Danese S, et al. *Lancet*. 2022;399:2113-2128. 2. U.S. Food & Drug Administration [FDA]. *FDA requires warnings about increased risk of serious heart-related events, cancer, blood clots, and death for JAK inhibitors that treat certain chronic inflammatory conditions*. FDA Website. 2021. https://www.fda.gov/drugs/drug-safety-and-availability/fda-requires-warnings-about-increased-risk-serious-heart-related-events-cancer-blood-clots-and-death

How Do We Put Together the Puzzle of Therapy Selection?

DRUG

Efficacy

Indication
Rapidity of onset
Durability
Pharmacokinetics/TDM
Combination vs. monotherapy
Positioning and sequence

Safety

Infection
Cancer
Specific concerns by agent or mechanism

PATIENT

Individual Characteristics

Age
Stages of disease
Comorbidities and other inflammatory conditions
Preferences
Access to treatment

Disease Characteristics

Disease behavior/complication
Disease severity
Early vs. late
EIMs
Treatment history

EIM = extraintestinal manifestation; TDM = therapeutic drug monitoring.

CME OUTFITTERS

Assessing UC Severity

Disease Activity

- Symptoms
  - GI and EIM
- Biomarkers of inflammation
  - CRP and FCP
- Endoscopic findings

Disease Severity

- Prior flare behavior
- Disease course since diagnosis

Risk Factors for Colectomy

- Age <40 years
- Extensive colitis
- Deep ulcers (Mayo 3 UCEIS > &)
- History of hospitalization
- High CRP/ESR
- *C. difficile* infection
- CMV infection

CMV, cytomegalovirus; CRP C-reactive protein; ESR, erythrocyte sedimentation rate; GI, gastrointestinal; UCEIS, Ulcerative Colitis Endoscopic Index of Severity

Peyrin-Biroulet L, et al. *Clin Gastroenterol Hepatol.* 2016;14(3):348-354.

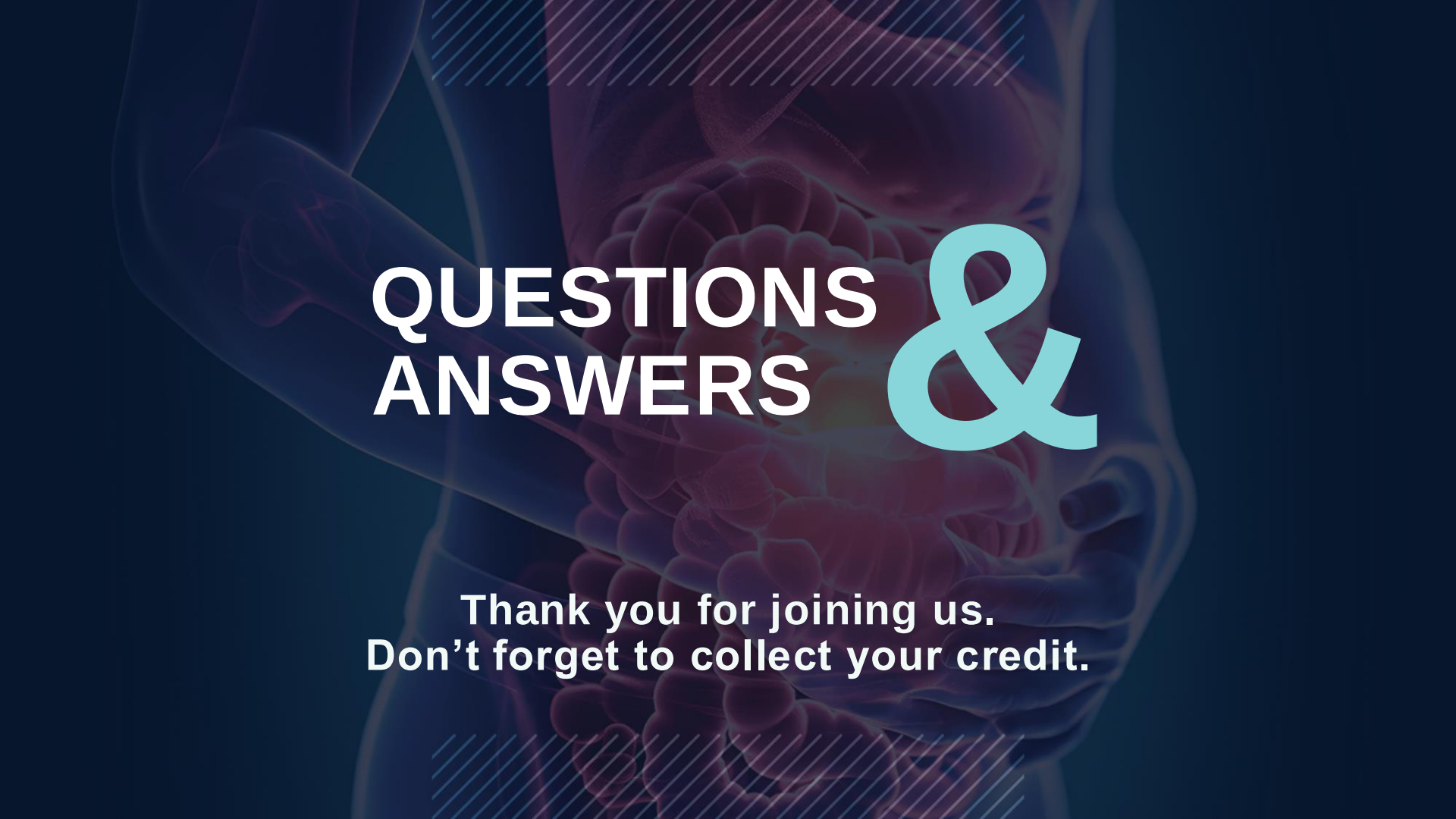
Impact of data on population health decisions

Faculty Discussion

SMART Goals

Specific, Measurable, Attainable, Relevant, Timely

- Overcome insurance-mandated barriers to treatment, such as prior authorizations, to increase remission rates and reduce disease-related hospitalizations and surgeries
- Incorporate methods to reduce the overall cost of treatment for patients and payors
- Identify patients for whom novel treatment options may be the best option to improve outcomes and reduce healthcare resource utilization
- Propose alternatives to increase access to treatment for uninsured patients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ANSWERS
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In-Person

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